# ANNALS

OF THE

# ROYAL COLLEGE OF SURGEONS OF ENGLAND

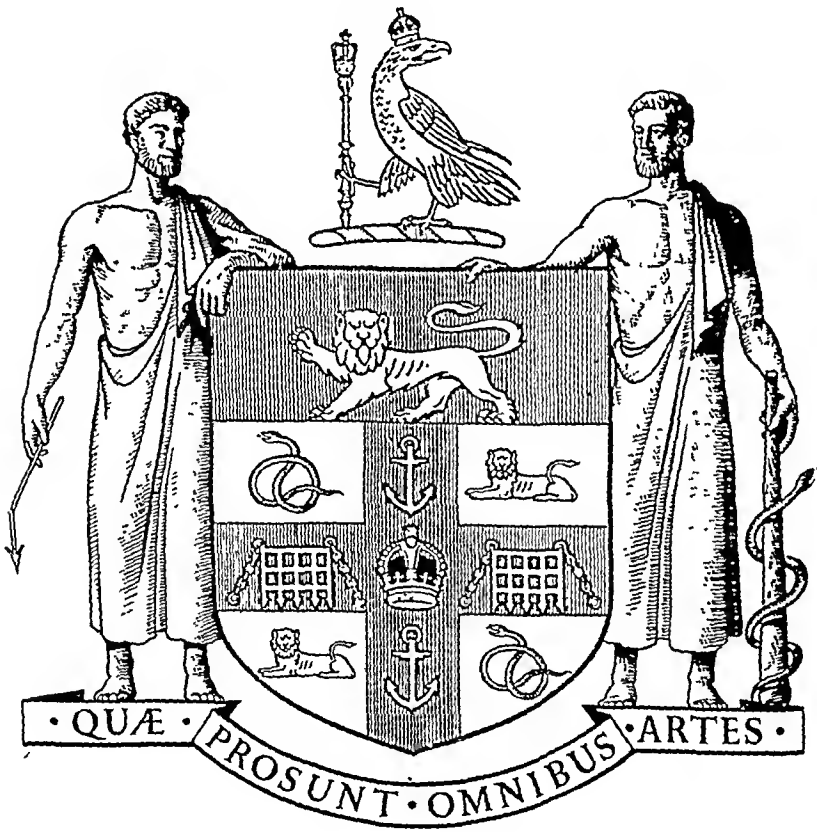
EDITOR: SIR CECIL WAKELEY, K.B.E., C.B., D.Sc., F.R.C.S., F.R.S.E.

---

VOLUME 4

---

JANUARY - JUNE 1949




*Published by*

THE ROYAL COLLEGE OF SURGEONS OF ENGLAND
LINCOLN'S INN FIELDS LONDON, W.C.2

# CONTENTS


| | | Page |
|---|---|---|
| Disordered Metabolisms in Thyrotoxicosis and Myxœdema | J. Douglas Robertson | 3 |
| Sayings of the Great | | 23 |
| Observations on the Appearances of Intestinal Tumours | Cuthbert E. Dukes | 24 |
| Malignant Diseases of the Paranasal Sinuses | F. C. W. Capps | 38 |
| Osteomyelitis of the Mandible | S. H. Wass | 48 |
| Zeis's Gland and Sebaceous Cysts in General | E. Wolff | 58 |
| "Observables" at the Royal College of Surgeons 13. A Bronze Écorché Statuette | | 60 |
| Monthly Dinners | | 63 |
| Diary for January | | 63 |
| Diary for February | | 64 |
| Bradshaw Lecture | L. E. C. Norbury | 65 |
| Sayings of the Great | | 89 |
| The Surgical Significance of the Unusual in the Pathology of Intestinal Tumours | Cuthbert E. Dukes | 90 |
| The Pathological and Physiological Aspects of Sterol Metabolism | E. C. Dodds | 104 |
| Sibert Forrest Cowell | | 121 |
| The Restoration and Development Fund | | 121 |
| "Observables" at the Royal College of Surgeons 14. The Rowlandson Water-Colours | | 122 |
| The Library John Hunter's Writings | | 123 |
| Monthly Dinners | | 125 |
| Diary for February and March | | 125 |
| Hunterian Oration for 1949 | H. S. Souttar | 127 |
| The Restoration and Development Fund | | 141 |
| John Hunter's Account of a "Mortifyd" Appendix Caeci | V. Zachary Cope | 142 |
| Sayings of the Great | | 143 |
| Wilfred Trotter | Julian Taylor | 144 |
| "Observables" at the Royal College of Surgeons 15. Pictures by George Stubbs, R.A. | | 160 |
| The Hunterian Dinner | | 164 |
| Observations on the Pathogenesis and Treatment of Skeletal Tuberculosis | M. C. Wilkinson | 168 |
| The Surgical Relief of Abdominal Pain by Splanchnic Block | M. L. Esnaurrizar | 192 |
| Monthly Dinners | | 194 |
| Diary for March | | 194 |
| Diary for April | | 195 |

Page

The Surgical Treatment of Carcinoma of the Pancreatoduodenal Area .. .. .. .. .. .. Richard Cattell 197
Facial Pain .. .. .. .. .. Sir Charles Symonds 206
Sayings of the Great .. .. .. .. .. .. .. 212
The Faculty of Anæsthetists .. .. .. .. .. .. 213
Pott's Disease and Pott's Paraplegia .. .. G. R. Girdlestone 214
The Pathology of Blunt Head Injury.. .. Keith Simpson 232
High Voltage X-Rays in the Treatment of Malignant Tumours at a Depth .. .. .. .. .. .. D. W. Smithers 242
"Observables" at the Royal College of Surgeons
16. The Arms of the Company and College .. .. .. .. 257
The Restoration and Development Fund .. .. .. .. 260
The Library
Vesalius and Lister .. .. .. .. .. .. .. 261
Monthly Dinners .. .. .. .. .. .. .. .. 265
Diary for April .. .. .. .. .. .. . .. 265
Diary for May .. .. .. .. .. .. .. .. 266
The Life and Achievements of Joseph Thomas Clover A. D. Marston 267
The Restoration and Development Fund .. .. .. .. 280
Early Stages of Human Development .. .. W. J. Hamilton 281
Congenital Obstruction at the Bladder Neck A. W. Badenoch 295
Sayings of the Great .. .. .. .. .. .. .. 307
The Problem of Closed Head Injury .. .. G. F. Rowbotham 308
The Female Breast and Its Development .. .. C. M. West 317
"Observables" at the Royal College of Surgeons
17. Records of Admiral Horatio Nelson's Wounds .. .. .. 326
Opening of Residential Quarters .. .. .. .. .. 328
The Library
Edward Jenner, born 17 May 1749. On the Cow Pox, the original paper .. .. .. .. .. .. .. .. 332
Monthly Dinners .. .. .. .. .. .. .. .. 335
Diary for May .. .. .. .. .. .. .. .. 335
Diary for June .. .. .. .. .. .. .. .. 336
John Hunter and His Museum .. .. ... F. Wood Jones 337
Some Observations on the Pathology and Surgical Treatment of Labyrinthine Vertigo of Non-Infective Origin T. Cawthorne 342
Surgical Problems Involved in Breast Cancer Frank E. Adair 360
Sayings of the Great .. .. .. .. .. .. .. 380
The Restoration and Development Fund .. .. .. .. 380
Malignant Disease of the Mouth .. .. Sir Stanford Cade 381
Liver Function Tests .. .. .. .. .. L. E. Glynn 392
The Honorary Medal of the College.. .. .. .. .. 399
"Observables" at the Royal College of Surgeons
18. The Jacksonian Prize .. .. .. .. .. .. 400
The Library
A Representative Exhibition .. .. .. .. .. .. 401
Monthly Dinners .. .. .. .. .. .. .. .. 403
Diary for June .. .. .. .. .. .. .. .. 403
Diary for July .. .. .. .. .. .. .. .. 404
Index to Volume 4 .. .. .. .. .. .. .. .. 405

# THE DISORDERED METABOLISMS IN THYROTOXICOSIS AND MYXŒDEMA

Lecture delivered at the Royal College of Surgeons of England

on

13th December, 1948

by

J. Douglas Robertson, M.D., D.Sc., F.R.C.P., F.R.I.C., D.P.H.

Director, Department of Clinical Investigation, The London Clinic, London, W.1

THYROTOXICOSIS AND MYXŒDEMA, or overactivity and underactivity of the thyroid gland, are diseases associated with many disordered metabolisms. Of these it is proposed to study disorders of the basal metabolism, calcium and phosphorus, carbohydrate, cholesterol, creatine and iodine.

## BASAL METABOLISM

*Thyrotoxicosis.* In true untreated thyrotoxicosis the basal metabolism is always raised above normal, and the greater the toxicity, the higher is the basal rate. As the level of the basal metabolism indicates the severity of the thyrotoxicosis, it follows that in mild cases the basal rate will not be greatly raised above the range of normal. It may even be within the generally accepted limits of normal healthy people. This has led many observers to misinterpret the basal metabolism findings. Thus if we assume that the normal range of the basal rate is plus 10 to minus 10, then if a suspected case of thyrotoxicosis gives an initial rate of plus 8, one would feel inclined to say that the case did not have a raised metabolism because it was within normal limits. But if the patient's true basal rate was minus 9—also within normal limits—then a reading of plus 8 would actually mean an increase of 17 per cent. above the patient's healthy normal reading. It is in such mild cases of thyrotoxicosis as these, often not obvious clinically, where a full investigation of the basal metabolism can give much help in diagnosis. It is important, however, first to study the action of iodine on the basal metabolism in thyrotoxicosis.

To begin with, it must be appreciated that iodine has no effect whatsoever on the basal metabolism of normal healthy people. But iodine has a specific action in lowering the raised metabolism of thyrotoxicosis —very rarely it may cause the basal rate to rise. Not only pure iodine itself, but all its soluble compounds have a similar action and this iodine effect appears to depend upon the amount of soluble iodide present. In Fig. 1 a list of salts and solutions of iodine in common use is given, with the amounts of total iodine present.

Fig. 1.

VARIOUS IODINE SALTS AND SOLUTIONS

| Iodine compound | Free Iodine | Salt of Iodine | Vehicle | Total Iodine (free iodine plus iodine in combination) in 1 minim |
|---|---|---|---|---|
| *Liquid*: | | | | |
| 1. Liq. iodi. mitis (B.P. 1932) or Tinct. iodine. | 2.5% | Potassium iodide 1.5% | Alcohol | 2.16 mgms. |
| 2. Liq. iodi. simplex (B.P. 1932) or Tinct. iodi. French Codex of 1908. | 9.0% | Nil | Alcohol | 5.33 mgms. |
| 3. Lugol's Solution (B.P. 1936) | 5.0% | Potassium iodide 10% | Water | 7.49 mgms. |
| 4. Hydriodic acid. | | Hydrogen iodide 10% | Water | 5.89 mgms. |
| *Solid*: | | | | 0.065 gram or 1 grain contains |
| Potassium iodide .. .. .. .. .. .. .. | | | | 49.6 mgms. |
| Sodium iodide .. .. .. .. .. .. .. | | | | 54.9 mgms. |
| Ethyl iodide .. .. .. .. .. .. .. | | | | 52.9 mgms. |
| Sajodin (calcium iodobehenate) .. .. .. .. .. | | | | 15.6 mgms. |

It can be calculated that 30 minims of Lugol's solution is roughly equivalent to 4½ grains of potassium iodide or 4 grains of sodium iodide. Any dose exceeding 6 mgms. of iodine daily (approximately 1 minim of Lugol's solution) will produce the maximum effect, but it is usual to give the equivalent of at least 15 minims of Lugol's solution per day. The action of iodine on the basal metabolism of thyrotoxicosis, over a period of twenty days, can vary from case to case and in the same case from time to time. There appeared to be four well-defined responses and these are shown in Figs. 2 to 5 (Robertson, Brit. Journ. of Surgery 1946). In Fig. 2 iodine brought about a maximum reduction in the basal metabolism to the patient's normal rate. In other words the toxicity was completely neutralised, and a successful subtotal thyroidectomy was unable to further lower the basal rate. In Fig. 3 iodine brought about only a partial fall in the basal metabolism which remained appreciably above normal. In Fig. 4 iodine caused a sharp fall followed at once by a sharp rise in the basal rate, the level after iodine being equal to or even exceeding the pre-iodine basal metabolism. In Fig. 5 iodine caused the basal metabolism to rise—this type of response is unusual in that an active case of thyrotoxicosis can be made clinically worse by iodine. These four well-defined curves are shown diagrammatically in Fig. 6.

Different views have been put forward to explain the varying effects of iodine on the basal metabolism in thyrotoxicosis. By some it is believed that the basal metabolism rises after iodine because the thyrotoxicosis becomes refractory to that drug. In other words, for some reason iodine loses its ability to control the disease. The treatment is to stop iodine for 4-6 weeks and begin it again when a favourable response might be obtained, as in Figs. 2 and 3. Others again do not believe in this double-edged action of iodine. They maintain that the variations in the basal rate are just part and parcel of the disease syndrome, that iodine cannot stop these variations, but it can make them take place at a lower level of metabolism. In other words, patients may have increasing thyrotoxicosis while taking iodine, but that is in spite of, not because of, the drug.

Whatever the true interpretation, from a practical point of view it can be stated that, over a period of twenty days, iodine affects the basal metabolism of thyrotoxicosis in four different ways, and that this action is specific for thyrotoxicosis. It does not occur in any other disease, nor in normal people.

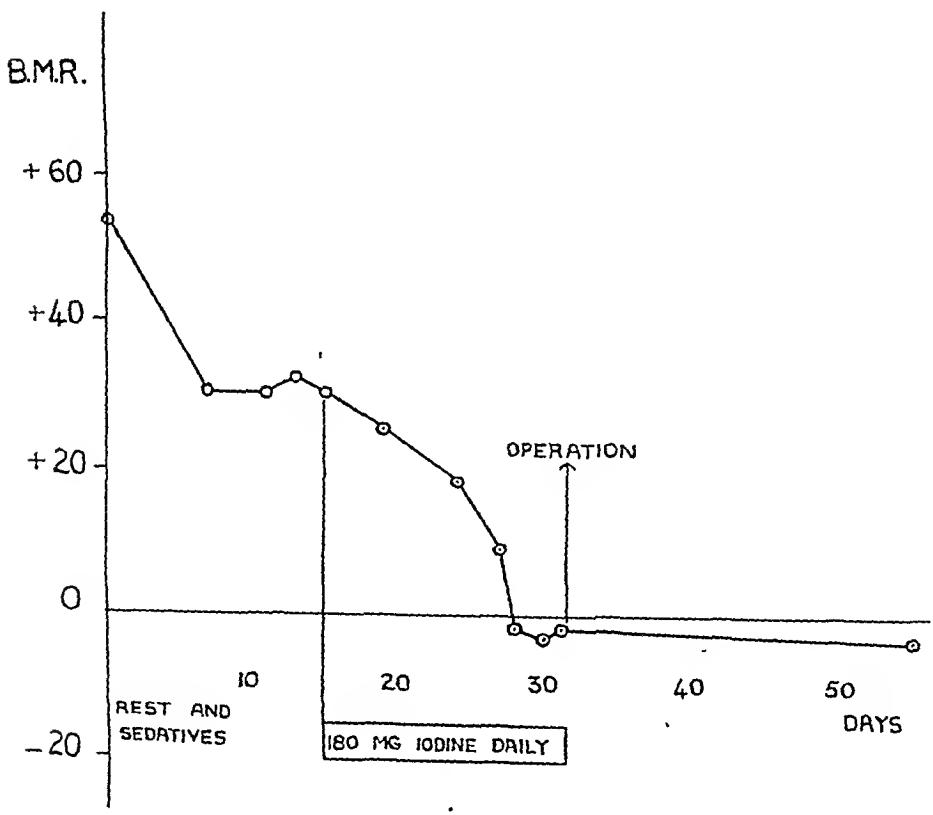



Fig. 2. Most favourable iodine response.

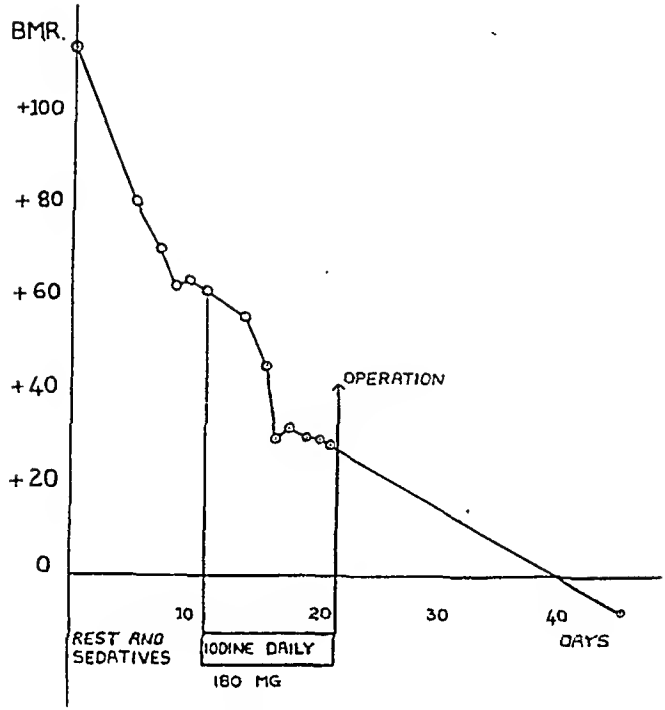



Fig. 3. Favourable iodine response.

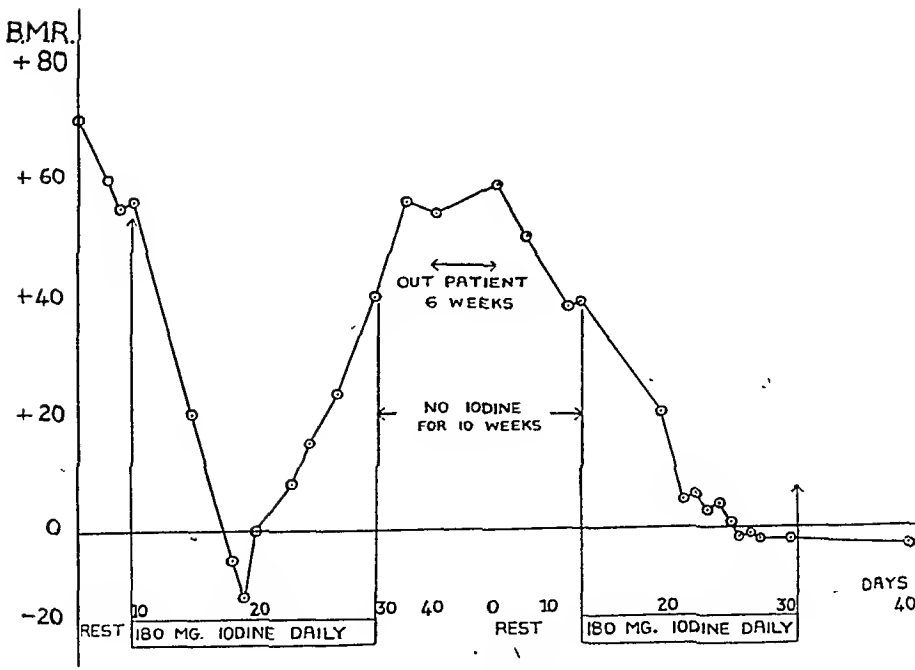



Fig. 4. Bad iodine response.

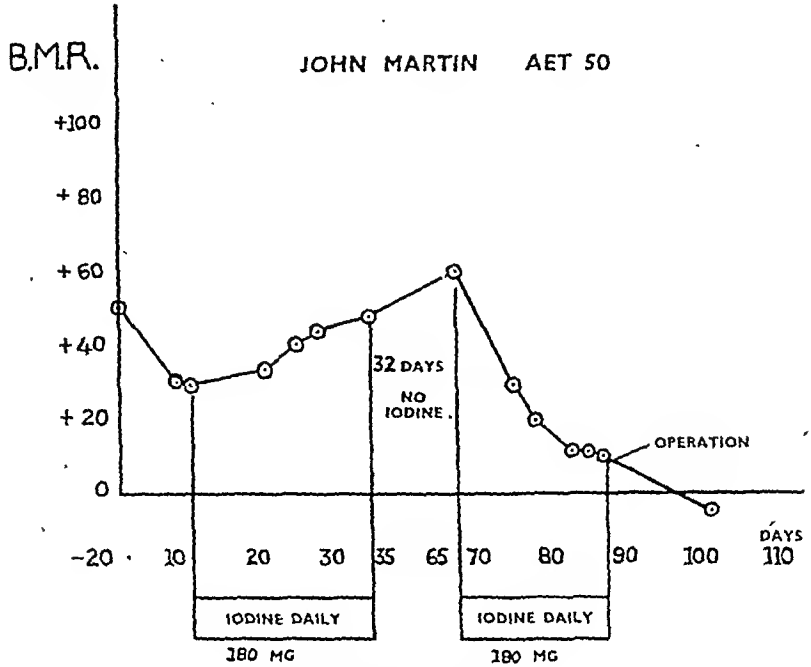



Fig. 5. Bad iodine response.

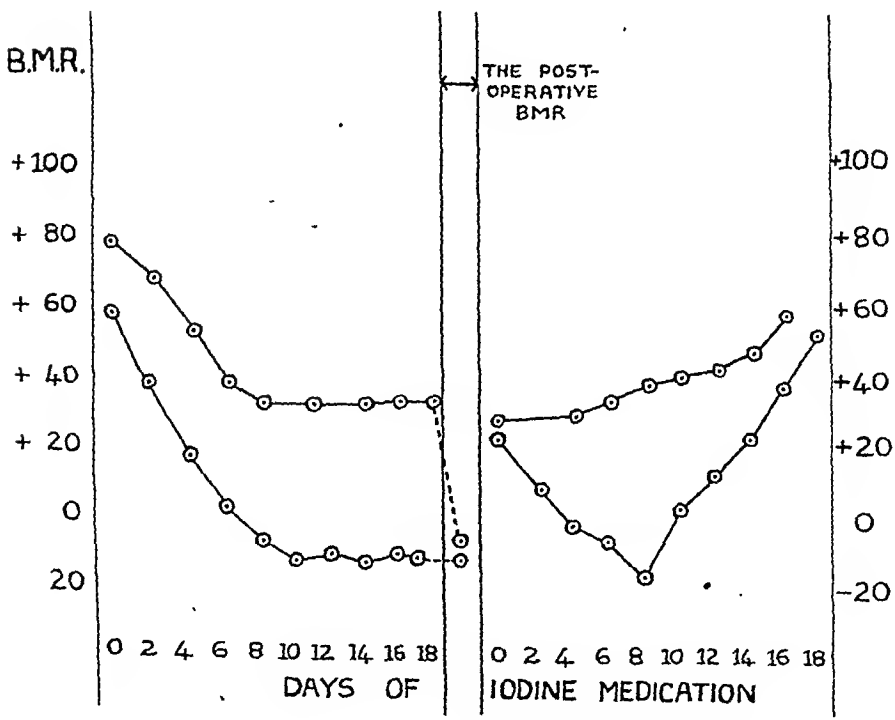



Fig. 6. The action of iodine on the basal metabolism of four cases of thyrotoxicosis.

This specific action of iodine can be used in the diagnosis of mild cases of thyrotoxicosis, where the initial basal metabolism is only slightly raised above normal, or even is within the normal range. In 1934 I investigated and published a most interesting case of mild thyrotoxicosis with an initial basal metabolism of minus 8. (Robertson, 1934.) After ten days of iodine the basal metabolism fell to minus 27. A surgeon unwillingly was persuaded to perform a subtotal thyroidectomy, but histologically the gland showed evidence of a toxic goitre. The post-operative basal rate was minus 25. There was no suggestion of myxœdema either after iodine or after the operation. Means (1933) has clearly discussed the diagnostic value of iodine in mild thyrotoxicosis as shown in Fig. 7.

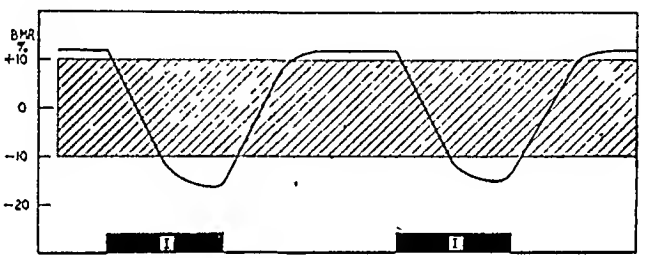



Fig. 7. Diagrammatic representation of iodine relationships in a case of genuine thyrotoxicosis but with initial metabolism little if at all above the standard zone. The fluctuations are diagnostic of thyrotoxicosis although the actual initial level would not be diagnostic of that state.

We see here a diagrammatic representation of the effects of iodine on the basal metabolism of a case of thyrotoxicosis, the actual initial level of which would not be diagnostic of that state. In addition to the fall in the metabolism, it is well to remember that the basal rate may also rise, or fall and rise.

Conditions other than thyrotoxicosis have a raised basal metabolism, such as leukæmia, polycythæmia vera, heart failure with dyspnœa and fever, but thyrotoxicosis is the only disease whose basal rate is affected by iodine.

*Myxœdema.* In myxœdema the basal metabolism is always diminished below normal, and very frequently it is in the region of minus 35 to minus 40. The frank case of myxœdema is usually very easy to recognise, for example Fig. 8, but the diagnosis of mild cases of hypothyroidism, where the basal metabolism is not greatly reduced and may be within the range of the lower limits of normal, may present difficulties.

In these types of cases the therapeutic or diagnostic value of thyroid may be tried in the same way that iodine is given in thyrotoxicosis. Fig. 9 shows the different response of normal, healthy, people and cases of myxœdema to a thyroid intake of two grains per day.

Fig. 8. A typical case of myxœdema.

In myxœdema there is an appreciable rise in the basal metabolism and pulse rate with loss of weight at the end of two and four weeks, but in the absence of hypothyroidism no significant alterations in the basal metabolism, pulse rate, or weight took place over a like period. There

Fig. 9. Normal Subjects and Cases of Myxœdema on Thyroid gr.ii. Daily for Two and Four Weeks

| | No. of cases | Basal Metabolism | | | Weight in lbs. | | | Basal Pulse Rate | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Thyroid gr. ii. daily | | | Thyroid gr. ii. daily | | | Thyroid gr. ii. daily | |
| | | Before | 2 wks. | 4 wks. | Before | 2 wks. | 4 wks. | Before | 2 wks. | 4 wks. |
| Myxœdema. | 8 | −35 | −22 | −17 | 155 | 151 | 149 | 52 | 61 | 64 |
| Normal subjects. | 6 | −11 | −10 | −11 | 143 | 142 | 143 | 68 | 70 | 68 |

is therefore a simple test for mild hypothyroidism if the initial basal metabolism is inconclusive and high enough to be within the normal range. It involves re-measuring the basal rate two weeks after a daily intake of two grains of thyroid. If the pulse rate and basal metabolism rise significantly, hypothyroidism is present; if thyroid medication has no effect, then hypothyroidism is absent.

The tolerance of thyroid by mouth and thyroxine intravenously in cases of myxœdema and subjects with a low metabolism, but without myxœdema, have been studied by Winkler and his colleagues. (Winkler, Criscuolo, Lavietes, 1943; Winkler, Lavietes, Robbins, 1943.) The cases with a low metabolism included obesity, arteriosclerosis, neuroses, alopecia, syphilis, infantilism, diabetes, and simple goitre. They were

able to take up to six grains of thyroid for several months without any elevation in the basal metabolism. Even the response to intravenous thyroxine was not nearly so well-marked as in myxœdema. They suggested as an explanation that subjects without myxœdema were able to inactivate thyroid substances given orally.

### Calcium and Phosphorus Metabolism

Next, a study of the calcium and phosphorus metabolisms which appear to become disordered in metabolic diseases of the thyroid gland. Of these, it is the calcium metabolism, probably, which is the primary factor. The part played by phosphorus is somewhat confused by reason of its association with protein catabolism, which is also deranged in metabolic disorders of the thyroid gland.

*Thyrotoxicosis.* It has been known for many years that thyrotoxicosis is associated with an excessive excretion of calcium, leading in long-standing cases to demonstrable decalcification of the skeleton, osteomalacia, and even pathological fracture of bones. Several theories have been put forward to explain this disordered calcium metabolism. It has been suggested that calcium is excreted in excessive amounts because:

1. The thyroid hormone (presumably secreted excessively in thyrotoxicosis) has a direct stimulating catabolic effect on the calcium deposits in the bones. (Aub, Bauer, Heath and Ropes, 1929.)

2. There is an associated hyperparathyroidism (Hansman, Wilson, 1934; Hansman, Carr-Fraser, 1938).

3. There is an increased basal metabolism, and that this, *per se*, increases the calcium metabolism and excretion (Aub, Bauer, Heath, Ropes, 1929.)

4. The calcium of the bones, in its capacity as a base, is used to neutralise the acid products resulting from an increased protein metabolism (Hoennicke, 1904.) Observations by Aub and his colleagues (Aub, Bauer, Heath, Ropes, 1929; Albright, Bauer, Aub, 1931) have indicated that the last two theories are unlikely. First, they have shown that the calcium excretion is normal in other diseases associated with a raised metabolism. Secondly, they have shown that calcium is not essential to aid the excretion of sulphates and phosphates, and so cannot explain its excessive mobilisation in thyrotoxicosis.

The altered calcium excretion in thyro-parathyroid diseases can best be studied by making a series of calcium balance experiments, first on normal subjects, and then in these diseases. On a low calcium intake, such as 100 mgms. per day, normal subjects have a urinary output of calcium which is less than the intake, and only a quarter of the total output. In other words, most of the calcium is excreted in the fæces and the amount exceeds the intake, due no doubt to the calcium excreted into the gut by the various gastro-intestinal juices. In both thyrotoxicosis and hyperparathyroidism the position is reversed—that means there is a

greatly increased calcium excretion in the urine far exceeding the calcium intake and also the amount of calcium lost in the fæces. I would like for a moment to discuss the fæcal loss of calcium in thyrotoxicosis and in hyperparathyroidism. It has been stated that in thyrotoxicosis there is a proportional increase in the calcium excretion in both the urine and the fæces, whereas in hyperparathyroidism the increase only takes place in the urine, the fæcal loss remaining normal. (Aub, Bauer, Heath, Ropes, 1929; Aub, 1928-9). These statements have been quoted from time to time in the literature, until it has become accepted that one of the pathognomonic features of thyrotoxicosis is an augmented fæcal loss of calcium. With great respect I do not think that these statements are quite accurate. I have abstracted and put together in a table the experimental findings of Aub and his colleagues (Bauer, Albright, Aub, 1930; Aub, Bauer, Heath, Ropes, 1929); (Hunter and Turnbull, 1931); (Bassett, 1935) and (Garlock, 1936). These findings are shown on Fig. 10. As the calcium intakes are approximately the same, the respective outputs are comparable. It will be seen that in both hyperparathyroidism and thyrotoxicosis there is a greatly increased urinary output of calcium. It is almost six times normal. Now if we look at the calcium loss in the fæces, we find that there is only one case where this greatly exceeds normal. In this case the fæcal output of calcium was three times the normal mean, but the urinary loss was fifteen times the normal mean and more than twice as much as any other case reported. All the other cases of thyrotoxicosis had a fæcal output of calcium within average normal limits. I have compared the two mean values of 0·6 g. for normals and 0·77 g. for thyrotoxicosis and found they have no significant difference. On the other hand, if a similar calculation is made for the fæcal output of calcium in hyperparathyroidism, the mean values of 0·6 g. for normals and 0·36 g. for hyperparathyroidism have a significant difference. It seems, therefore, that in conflict with current opinion, in thyrotoxicosis the fæcal output of calcium is normal, and in hyperparathyroidism it is diminished, whereas in both diseases there is an equal increase in the calcium output in the urine.

It is well known that iodine causes a symptomatic improvement in thyrotoxicosis and a fall in the basal metabolism—this is associated with a diminution in the excessive calcium loss in the urine. A successful thyroidectomy results in a return of the calcium excretion to normal.

A study of the serum calcium in thyrotoxicosis throws more light on the cause of the increased loss of calcium in the urine. Despite lack of agreement among various writers, I found the serum calcium to be low in thyrotoxicosis with a mean value of 9·7 mgms. per cent. (range of 9·1 to 10·8) as compared with a normal mean of 10·4 mgms. (range 9·9 to 11·1).

We can assume that whatever causes the excessive loss of calcium in the urine, also causes the level in the blood to fall or vice versa.

*Myxœdema.* If we now turn to myxœdema we note findings in direct contrast to those found in thyrotoxicosis. The fæcal loss of calcium is again normal, but the output in the urine is diminished well below normal. Adequate thyroid medication causes the well known symptomatic improvement and rise in basal metabolism and this is accompanied by a rise in the urinary excretion of calcium. In the blood thyroid feeding causes *a fall in the calcium level from a high normal to a figure below normal.*

Fig. 10

| Calcium intake | | | Urinary output calcium | | | Fæcal output calcium | | |
|---|---|---|---|---|---|---|---|---|
| Normals | Hyperparathyroidism | Thyrotoxicosis | Normals | Hyperparathyroidism | Thyrotoxicosis | Normals | Hyperparathyroidism | Thyrotoxicosis |
| 0.31 | 0.3 | 0.32 | 0.20 | 1.5 | 0.68 | 0.44 | 0.52 | 0.85 |
| 0.21 | 0.45 | 0.21 | 0.11 | 1.42 | 2.92 | 0.38 | 0.59 | 1.82 |
| 0.31 | 0.3 | 0.31 | 0.30 | 0.68 | 1.39 | 0.41 | 0.24 | 0.71 |
| 0.29 | 0.3 | 0.29 | 0.05 | 1.36 | 1.08 | 0.49 | 0.24 | 0.69 |
| 0.34 | 0.3 | 0.28 | 0.06 | 0.5 | 1.04 | 0.39 | 0.38 | 0.56 |
| 0.38 | 0.31 | 0.32 | 0.2 | 1.31 | 0.65 | 0.55 | 0.19 | 0.5 |
| 0.28 | 0.38 | 0.34 | 0.23 | 0.81 | 0.38 | 0.65 | 0.43 | 0.58 |
| 0.33 | 0.3 | 0.24 | 0.04 | 0.77 | 0.81 | 0.86 | 0.3 | 0.45 |
| 0.38 | — | — | 0.09 | — | — | 0.71 | — | — |
| 0.39 | — | — | 0.24 | — | — | 0.96 | — | — |
| 0.34 | — | — | 0.27 | — | — | 0.31 | — | — |
| 0.35 | — | — | 0.46 | — | — | 0.44 | — | — |
| 0.26 | — | — | 0.38 | — | — | 0.33 | — | — |
| Mean 0.33 | 0.33 | 0.29 | 0.19 | 1.04 | 1.12 | 0.6 | 0.36 | 0.77 |

Comparison of differential calcium excretion in normals, hyperparathyroidism, and thyrotoxicosis. (Results expressed in grammes per three days.)

The two mean values 0.60 for normals and 0.77 for thyrotoxicosis are not significantly different. $t=1.27$; P is greater than 0.2.

The two mean values 0.60 for normals and 0.36 for hyperparathyroidism are significantly different. $t=3.2$; P is less than 0.01.

A summary may now briefly be made of the disturbed calcium metabolism in thyrotoxicosis and myxœdema:

1. In thyrotoxicosis the calcium loss in the urine is excessive; it is normal in the fæces. After a successful sub-total thyroidectomy, the calcium metabolism returns to normal. The serum calcium is low in thyrotoxicosis and rises to normal after successful operation.
2. In myxœdema the calcium loss in the urine is diminished; it is normal in the fæces. After adequate thyroid feeding the calcium metabolism returns to normal. The serum calcium is slightly raised in myxœdema, and falls after thyroid feeding.

As to the cause of the disturbed calcium metabolism, I do not think that the two theories previously suggested are satisfactory.

*Aub's theory* that the excessive secretion of the thyroid hormone has a direct stimulating catabolic effect on the calcium deposits in bone, demands a raised serum calcium in thyrotoxicosis, or at least normal, depending on whether the excretion of calcium can keep pace with its mobilisation. But the serum calcium is diminished in thyrotoxicosis.

*Hansman's theory* that an associated hyperparathyroidism is present, also demands a raised or a normal serum calcium. Further we have seen that the calcium findings in thyrotoxicosis and hyperparathyroidism are quite different—the fæcal loss is normal in the first, but diminished in the second. As an alternative theory I have suggested (Robertson, 1942) that in thyrotoxicosis an excessive thyroid secretion acts directly on the kidneys and lowers its threshold for calcium. This causes a fall in the serum calcium, and as a result there is an increased mobilisation of calcium from the bones in an attempt to raise the diminished serum calcium. Conversely in myxœdema a diminished thyroid secretion raises the renal threshold for calcium, and the calcium output in the urine falls below normal. In other words I believe that the mechanism for the disturbed urinary loss of calcium in thyroid disease is a *vis-a-fronte*, as opposed to a *vis-a-tergo* suggested by the theories of Aub and his colleagues, and Hansman and his colleagues.

## CARBOHYDRATE METABOLISM

Thirdly, we come to a study of the carbohydrate metabolism in thyrotoxicosis. This can be discussed under two headings (*a*) Glycosuria and (*b*) an intolerance to galactose.

*Glycosuria.* This is not an uncommon finding in thyrotoxicosis. It has led to a study of the glucose tolerance test in the hopes that a curve

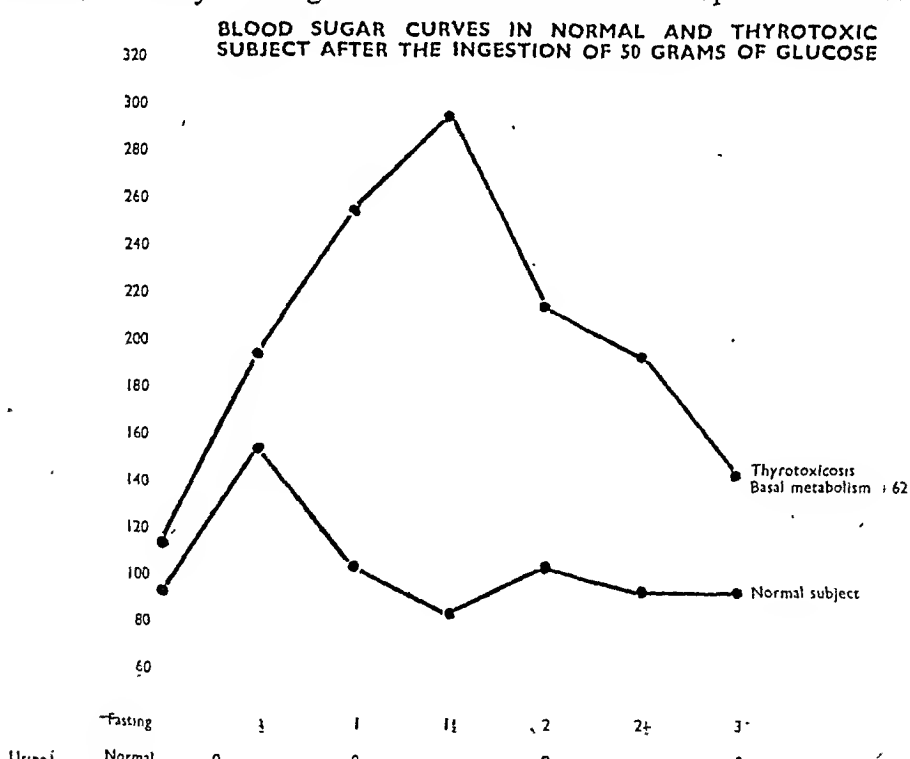



Fig. 11

significantly different from that found in diabetes might be obtained. But in fact both curves are alike, and this has led to a certain amount of controversy as to whether true diabetes is or is not commonly present in thyrotoxicosis. Fig. 11 shows a typical curve of the blood sugar following a twelve hours' fast and after the ingestion of 50 grammes of glucose in a case of severe thyrotoxicosis. The curve of a normal subject is also charted. The case of thyrotoxicosis might well be one of diabetes.

Several theories have been put forward to explain this intolerance to glucose, which, in the absence of diabetes, invariably disappears after a successful thyroidectomy. Thus it is believed:

1. That there is faulty oxidation of glucose such as occurs in diabetes (John, 1927). Against this, it has been stated that people with pure thyrotoxicosis have no defective oxidation of carbohydrate, but on the contrary they utilise sugar with marked ability, as shown by a respiratory quotient in the region of 1·00, and an increase in the heat production due to the specific dynamic action of the ingested sugar (Rabinowitch, 1931).
2. That there is a defective storage or a reduced deposition of carbohydrate as glycogen. It is known that thyroid feeding empties the liver of glycogen. (Sanger & Hun, 1922.)
3. That there is an excessive secretion of adrenalin (Rabinowitch, 1931).
4. That the diminution in the tolerance to glucose is similar in nature to that found in normal people on a starvation or low carbohydrate diet. This theory has been extended and a relationship drawn between the degree of intolerance to glucose and loss of body weight. (Hatlehol, 1932.)
5. That it is due to increased intestinal absorption of sugars. (Althausen, Lockhart, Soley, 1940.)
6. And lastly, that it is an indication of liver damage. (Youmans and Warfield, 1926).

In summary we can say that the cause of the reduced glucose tolerance in thyrotoxicosis still remains unsettled. It seems clear that there is no relationship between the elevation of the basal metabolism and the height of the hyperglycæmia; for example, a case of thyrotoxicosis with a basal metabolism of plus 90 gave a normal glucose tolerance curve, whereas a case with a basal metabolism of plus 27 gave the highest and the most prolonged hyperglycæmia.

Despite these anomalies and whatever the true nature of the hyperglycæmia in thyrotoxicosis may be, most observers agree that a high carbohydrate intake is an essential part of the treatment, and that the glycosuria is not of diabetic origin.

*Intolerance to Galactose.* We next come to a study of the metabolism of galactose in thyrotoxicosis (Althausen, Wever, 1937; Althausen, Lockhart, Soley, 1940; Maclagan and Rundle, 1940). The test is easily carried out and consists in giving the patient forty grammes of galactose by mouth after a twelve hour fast, then estimating the blood galactose at

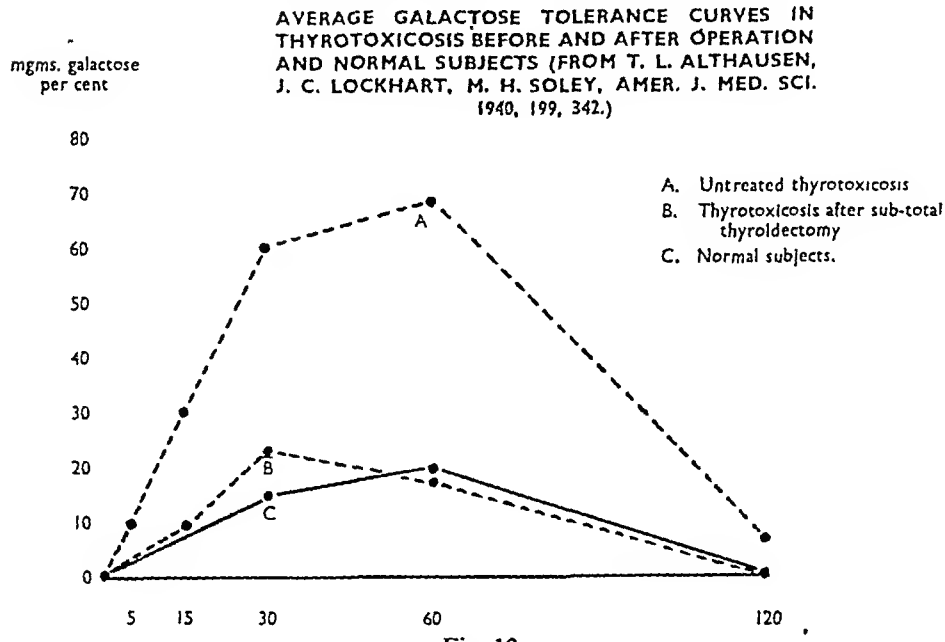



Fig. 12

5, 15, 30, 60, and 120 minutes afterwards. Fig. 12 shows the average galactose tolerance curves in normal people and cases of thyrotoxicosis before and after operation.

In normal people the blood galactose reaches a maximum of almost 20mgms. per cent. in an hour, and very small amounts were found in 5 and 120 minutes. In thyrotoxicosis the blood galactose reached a maximum of almost 70mgms. per cent. in an hour, and appreciable amounts were found in the five-minute period, while after successful subtotal thyroidectomy the curve reverted to normal. It is interesting to note that the galactose tolerance curve is normal in anxiety states, heart failure, hypertension, non-toxic goitre and other conditions simulating the syndrome of thyrotoxicosis. Blood galactose curves similar to those found in thyrotoxicosis are found in hepatic insufficiency and Paget's disease.

In myxœdema the blood galactose curve is lower than normal, the average peak just exceeding 2mgms. per cent. and in some cases no galactose can be detected in the blood at all.

Two explanations are possible in explaining the galactose metabolism in thyrotoxicosis. First, it may be an indication of liver injury which is known to occur in some cases of thyrotoxicosis. Secondly, it may be due to an increased intestinal absorption of glucose due to the excessive secretion of the thyroid hormone in thyrotoxicosis.

## CHOLESTEROL METABOLISM

Cholesterol is an unsaturated secondary alcohol, insoluble in water, and is not a true lipoid although associated with fat metabolism.

Apparently only a part of the blood cholesterol is derived from ingested food, most of it is synthesised within the body, probably in the liver and the suprarenal (Thanhauser and Magendantz, 1938). The normal blood serum cholesterol is given as 180-220 mgms. per cent.

*In myxœdema* the blood cholesterol is raised well above normal, and figures as high as 667 and 926 mgms. per cent. have been recorded (Craig, Lesser, Soley, 1944). Although Means has stated that it is possible to have full-blown myxœdema without any elevation of the cholesterol, most observers do not agree; for example, it has been stated (Gildea, Mann, Peters, 1939) that a cholesterol below 275 mgms. per cent. excludes a diagnosis of myxœdema. There appears to be a reciprocal relationship between the basal metabolism and the serum cholesterol, and as the basal metabolism rises after thyroid feeding, so the cholesterol falls.

The reason why the serum cholesterol is raised is by no means clear, but several theories have been put forward such as :

1. Cholesterol is retained in the blood stream because there is poor elimination in a diminished biliary excretion. Apparently the cholesterol content of bile is below normal in myxœdema (Hurxthal and Hant, 1934).
2. There is an increased synthesis of cholesterol.
3. It is due to a decrease in the blood volume which is known to be present in myxœdema (Thompson, 1926 ; Gibson and Harris, 1939).
4. It may be due to a compensatory mechanism whereby the organism mobilises fatty acids, cholesterol and lecithin, in an effort to increase the colloid osmotic pressure of the plasma, and so rid the tissues of their excessive fluid.

Although a reciprocal relationship between the basal metabolism and the serum cholesterol is present in myxœdema before and during treatment with thyroid, changes in the blood cholesterol are not due to changes in the basal metabolism, and vice versa. Thus the serum cholesterol is normal in cases with a diminished metabolism in the absence of myxœdema. Also the serum cholesterol may be raised when the basal metabolism is normal such as in diabetes, arteriosclerotic and hypertensive heart failure, pregnancy and obstructive jaundice. It seems likely that both hypercholesterolæmia and the low basal metabolism result from the myxœdema. This is supported by the fact that it is possible to alter one and not the other. Thus the basal metabolism of a case of myxœdema was raised as high as plus 40 with dinitro-ortho-cresol (a metabolic stimulant of the nitrophenol group) yet the myxœdematous appearance remained unchanged, (Dodds and Robertson, 1933), nor did it alter the cholesterol level (Cutting, Ryland, Tainter, 1934). Fig. 13 shows a case of myxœdema whose metabolism was raised to plus 40 by dinitro-o-cresol from an initial basal rate of minus 35. Fig. 14 is the same subject with a basal rate of only minus 4 on thyroid.

*In thyrotoxicosis* the blood cholesterol is lowered and it returns to normal after successful subtotal thyroidectomy.

## CREATINE METABOLISM

*Creatine* is found almost entirely in muscle and a large part of it is in combination with phosphorus as phospho-creatine or phosphogen. Creatine is present in blood, but it is believed to be normally absent from the urine in the adult except during menstruation and lactation. Creatinuria is found in excessive amounts in fever, thyrotoxicosis, wasting diseases, starvation, diabetes, and the muscular atrophies and dystrophies. Thyroid feeding produces a spontaneous creatinuria. The excretion of creatine in large amounts is believed to be due to an inability to synthesise

Fig 13 Case of Myxœdema where the metabolism was raised to plus 40 by dinitro-o-cresol from an initial basal rate of minus 35

Fig. 14
The same case as seen in Fig. 13 with a basal rate of minus 4, on thyroid.

phosphocreatine which is essential for muscular activity. The muscular weakness of thyrotoxicosis may then be explained.

*Creatinine* as opposed to creatine is a normal constituent of the urine and the output is very constant. Creatinine is an end-product of creatine metabolism, and is simply a waste product. If creatinine is ingested it is completely excreted, as opposed to creatine which is normally, to a large extent, retained.

Investigations into the creatine metabolism in thyrotoxicosis have been carried out by several authors; (Palmer, Carson, Sloan, 1928; Thorn, 1936; Richardson and Shorr, 1935; Sohval, King, Reiner, 1938), and I am borrowing freely from their findings.

In examining a case of suspected thyrotoxicosis it is suggested that two procedures are carried out:

1. The output of creatine in 24 hours after being 3 days on a creatine-free diet. It is abnormal if this exceeds 100 mgms. in 24 hours.

2. The output of creatine in 24 hours after the ingestion of 1·32 g. of creatine hydrate (equivalent to 1 gramme of creatine in urine). It is abnormal if less than 70 per cent. is retained by the body. For example, we may take the following case of thyrotoxicosis:

1. Excretion in 24 hours on creatine free diet = 0·2 g.
2. Excretion in 24 hours after ingestion of 1·32 g. of creatine hydrate = 1·0 g.

Excretion is 1·0—0·2=0·8 g. or 80 per cent. of amount ingested. This means retention of 20 per cent. only.

Fig. 15 shows the creatine retention in a case of thyrotoxicosis before and after treatment. Iodine causes marked diminution of creatinuria.

OBSERVATIONS ON THE CREATINE METABOLISM OF TWELVE CASES OF THYROTOXICOSIS (FROM G. W. THORN, ENDOCRINOLOGY, 1936, 20, 628)

| | Before treatment | After iodine therapy | 47 days after subtotal thyroidectomy |
|---|---|---|---|
| Basal metabolism .. .. .. | +50% | +20% | + 5% |
| Creatinuria, gm. .. .. .. | 0.210 | 0.077 | 0.115 |
| Creatine-tolerance (% retention) .. | 58% | 74% | 72% |

Fig. 15

In myxœdema there is no creatinuria and as much as 95 per cent. of ingested creatine is retained. *Thyroid feeding* causes creatinuria within 48 hours and before the basal metabolism rises.

## IODINE METABOLISM

Iodine is a normal constituent of the blood, but it is present in very small amounts, the normal range being 8 to 16 gamma or micrograms—that is ·008 to ·016 mgm. per cent. with a mean of 12 gamma. Among the first workers to make a study of the iodine metabolism in thyrotoxicosis was Holst and his colleagues in Norway (Holst, 1928; Holst, Lunde, Closs, Pederson, 1928; Holst, Lunde, 1929), who considered that the blood iodine consisted of two separate fractions.

First, the alcohol soluble or inorganic form which would vary with the intake of iodine or iodides.

Secondly, the alcohol insoluble or organic form which would contain the active principle of the thyroid secretion. These workers suggested

that the well known beneficial effects of the administration of Lugol's solution in thyrotoxicosis was explained by an inhibition in the secretion of the thyroid hormone, and they maintained they could demonstrate this in the blood. Thus as the alcohol soluble fraction in the blood rose because of iodine medication, so the alcohol insoluble fraction containing the thyroid hormone fell. Using the modified chemical methods of Holst and his co-workers we made a study of forty cases of thyrotoxicosis (Dodd, Lawson, Robertson, 1932). It was found that the blood iodine was increased in thyrotoxicosis affecting chiefly if not only the fraction which was insoluble in alcohol, and that the administration of iodine by mouth caused this fraction to fall. Such a case is shown in Fig. 16, where it is seen that the normal organic iodine is 4 gamma per cent. and the total iodine 14 gamma.

In this case of severe thyrotoxicosis with a basal metabolism of plus 80, the organic iodine was almost 40 gamma per cent. Thirty minims of Lugol's iodine daily caused the basal metabolism to fall to plus 30 and the organic iodine to 16 gamma per cent., and subtotal thyroidectomy to 12 gamma when the basal metabolism was normal.

In contrast to these findings however, it was found that the organic iodine did not always fall *pari passu* with the basal metabolism, nor was

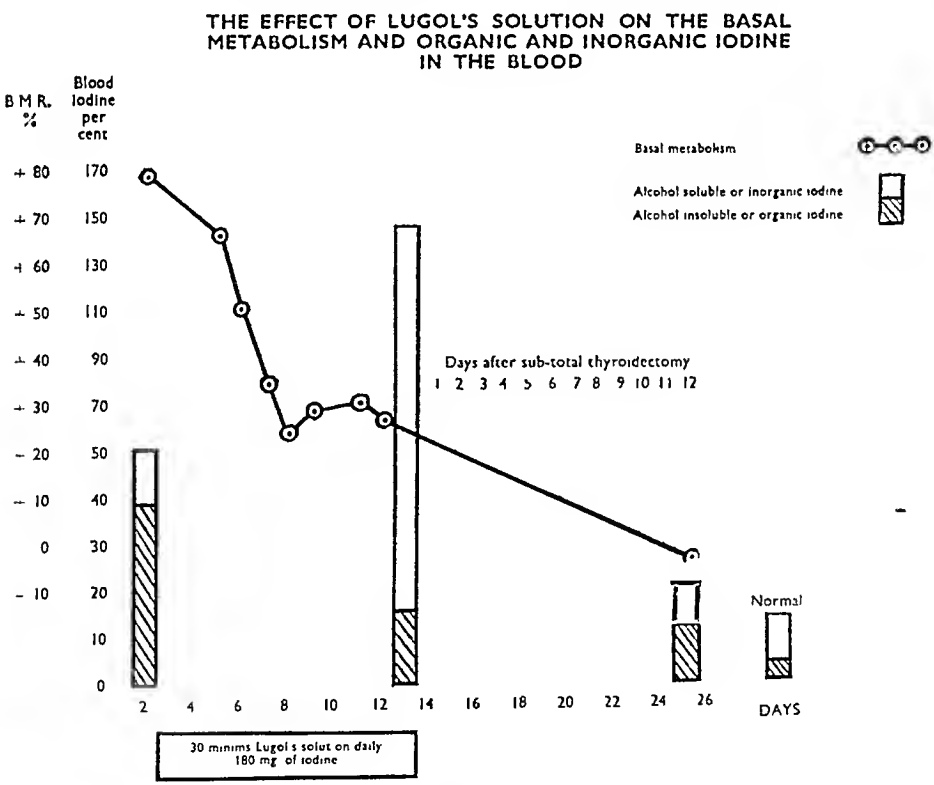



Fig. 16

the highest basal metabolism associated with the highest blood organic iodine. Again, non-toxic goitres were found to have increased organic iodine about three times normal, although about half that found in thyrotoxicosis. It was felt therefore that the alcohol insoluble or organic iodine was not necessarily an indication of the thyroid secretion.

In view of the difficult chemical procedure, and the uncertainty of interpreting organic or alcohol insoluble blood iodine in terms of thyroid secretion, subsequent workers only estimated the total blood iodine or chose other means of detecting abnormalities in the iodine metabolism in thyrotoxicosis. Briefly their findings were:

1. If small amounts of Lugol's solution containing 250 gamma of iodine per kilogram of body weight, that is about 12 minims of Lugol's solution or 15 mgms. of iodine, is injected intravenously, at the end of six hours normally 18 per cent. of injected iodine is present in the blood, in thyrotoxicosis there is none, and in myxœdema 30 per cent. (Watson, 1936). After such an injection the iodine output in the urine is greatest in thyrotoxicosis and least in myxœdema (Elmer, 1934).

2. On a normal diet the normal urinary excretion of iodine is 51 gamma in 24 hours, in thyrotoxicosis it is 184 gamma (Curtis and Puppel, 1937).

SUMMARY OF METABOLIC DISORDERS IN THYROTOXICOSIS AND MYXŒDEMA

| | Normal | Thyrotoxicosis | Myxœdema |
|---|---|---|---|
| *Basal Metabolism* .. .. .. .. | Normal | Raised | Diminished |
| Effect of iodine on B.M.R. .. .. | No action | Falls | — |
| Effect of thyroid on B.M.R. .. .. | No action | — | Rises |
| *Calcium Metabolism:* | | | |
| Serum calcium mgms. per cent. .. | 10.4 | 9.7 | 10.5 |
| On low calcium intake { Urine .. | 0.19 | 1.12 | 0.11 |
| Output in g. in 3 days { Fæces .. | 0.60 | 0.77 | 0.50 |
| *Carbohydrate Metabolism:* | | | |
| Peak hyperglycæmia after glucose ingestion in mgms. per cent. .. .. | 160 | >200 | <160 |
| Peak blood galactose after galactose ingestion in mgms. per cent. .. .. | 20 | 80 | 4 |
| *Cholesterol Metabolism:* | | | |
| Blood cholesterol mgms. per cent. .. | 180 | >150 | <275 |
| *Creatine Metabolism:* | | | |
| Creatinuria in mgms. in 24 hours .. | <100 | >100 | Absent |
| *Iodine Metabolism:* | | | |
| Blood iodine gamma per cent. .. .. | 12 | 27 | 3 |
| Blood iodine 6 hours after intravenous iodine .. .. .. .. .. | 18% | Nil | 30% |
| Urinary excretion of iodine .. .. | — | High | Low |

Fig. 17

3. On a low iodine intake of 87 gamma per day normally there is a negative balance of 123 gamma. In thyrotoxicosis this is increased to 317 gamma (Puppel and Curtis, 1938).

4. There would appear to be a correlation between the blood iodine level and the duration of the thyrotoxicosis. Thus (a) the blood iodine is raised in the early stages of the disease up to nine months, (b) the blood iodine falls to normal if the duration of the disease is one year or longer (H. J. Perkin, Lahey, 1938).

5. The recurrence or persistence of thyrotoxicosis is more likely to occur if the blood iodine is normal or low, and in these cases a more radical subtotal thyroidectomy should be carried out (Perkin, Cattell, 1939).

6. After the ingestion of 6 minims of Lugol's solution the blood iodine in normal people rises from about 8 mg. per cent. to over 100 mg. per cent., whereas in thyrotoxicosis the peak level of blood iodine rarely exceeds 80 mg. per cent. (Perkin, Lahey, 1937).

## Conclusions

In conclusion a summary of the metabolic disorders met with in diseases of the thyroid gland is given in Fig. 17.

## REFERENCES


ALBRIGHT, F., BAUER, W., and AUB, J.C. (1931) *J. Clin. Invest.* **10**, 187.

ALTHAUSEN, T. L., LOCKART, J. C., and SOLEY, M. H. (1940) *Amer. J. Med. Sci.* **199**, 342.

ALTHAUSEN, T. L., and WEVER, G. K. (1937) *J. Clin. Invest.* **16**, 257.

AUB, J. C. (1928-29) *Harvey Lectures* **24**, 151.

AUB, J. C., BAUER, W., HEATH, C., and ROPES, M. (1929) *J. Clin. Invest.* **7**, 97.

BASSETT, S. H. (1935) *J. Nutrition* **9**, 323.

BAUER, W., ALBRIGHT, F., and AUB, J. C. (1930) *J. Clin. Invest.* **8**, 229.

CRAIG, L. S., LISSER, H., and SOLEY, M. H. (1944) *J. Clin. Endocrinol.* **4**, 12.

CURTIS, G. M., and PUPPEL, I. D. (1937) *Arch. Int. Med.* **60**, 498.

CUTTING, W. C., RYLAND, D. A., and TAINTER, M. L. (1934) *J. Clin. Invest.* **13**, 547.

DODDS, E. C., LAWSON, W., and ROBERTSON, J. D. (1932) *Lancet* **2**, 608.

DODDS, E. C., and ROBERTSON, J. D. (1933) *Lancet* **2**, 1197.

ELMER, A. W. (1934) *Endocrinology* **18**, 487.

GARLOCK, J. H. (1936) *Ann. Surg.* **108**, 347.

GIBSON, J. G., and HARRIS, A. W. (1939) *J. Clin. Invest.* **18**, 59.

GILDEA, E. F., MANN, E. B., and PETERS, J. P. (1939) *J. Clin. Invest.* **18**, 739.

HANSMAN, F. S., and CARR FRASER, W. A. (1938) *J. Clin. Invest.* **17**, 543.

HANSMAN, F. S., and WILSON, F. H. (1934) *Med. J. Austral.* **1**, 37.

HATLEHOL, R. (1932) *Acta Med. Scand.* **77**, 558.

HOENNICKE, E. (1904) *Berl. Klin. Wschr.* **41**, 1154.

HÓLST, J. (1928) Die pathogenetischen Grundlagen der Thyreotoxikosetherapie. *Skr. norske Vidensk. Akad.* Matem. Naturv. Klasse No. 5.

HOLST, J., and LUNDE, G. (1929) *Amer. J. Surg.* **7**, 39.

HOLST, J., LUNDE, G., CLOSS, K., and PEDERSEN, O. C. (1928) *Klin. Wschr.* **7**, 2287.

HUNTER, D., and TURNBULL, H. M. (1931) *Brit. J. Surg.* 19, 203.
HURXTHAL, L. M., and HANT, H. (1934) *Ann. Int. Med.* 53, 825.
JOHN, H. J. (1927) *Endocrinology* 11, 497.
MACLAGAN, N. F., and RUNDLE, F. F. (1940) *Quart. J. Med.* 9, 215.
MEANS, J. H. (1933) *Ann. Int. Med.* 7, 439.
PALMER, W. M., CARSON, D. A., and SLOAN, L. W. (1928) *J. Clin. Invest.* 6, 597.
PERKIN, H. J., and LAHEY, F. H. (1938) *Arch. Int. Med.* 61, 875.
PERKIN, H. J., and CATTELL, R. B. (1939) *Surg. Gynec. & Obstet.* 68, 744.
PERKIN, H. J., and LAHEY, F. H. (1937) *New Engl. J. Med.* 216, 501.
PUPPEL, I. D., and CURTIS, G. M. (1938) *Arch. Int. Med.* 26, 1093.
RABINOWITCH, I. M. (1931) *Ann. Int. Med.* 4, 881.
RICHARDSON, H. B., and SHORR, E. (1935) *Trans. Assoc. Amer. Phys.* 50, 156.
ROBERTSON, J. D. (1934) *Lancet* 2, 1076.
ROBERTSON, J. D. (1942) *Lancet* 1, 672.
ROBERTSON, J. D. (1946) *Brit. J. Surg.* 34, 194.
SANGER, B. J., and HUN, E. G. (1922) *Arch. Int. Med.* 30, 397.
SOHVAL, A. R., KING, F. H., and REINER, M. (1938) *Amer. J. Med. Sci.* 195, 608.
THANNHAUSER, S. J., and MAGENDANTZ, H. (1938) *Ann. Int. Med.* 11, 1662.
THOMPSON, W. O. (1926) *J. Clin. Invest.* 2, 477.
THORN, G. W. (1936) *Endocrinology* 20, 628.
WATSON, E. M. (1936) *Endocrinology* 20, 358.
WINKLER, A. W., LAVIETES, P. H., ROBBINS, C. L., and MAN, E. B. (1943) *J. Clin. Invest.* 22, 535.
WINKLER, A. W., CRISCUOLO, J., and LAVIETES, P. H. (1943) *J. Clin. Invest.* 22, 531.
YOUMANS, J. B., and WARFIELD, L. M. (1926) *Arch. Int. Med.* 37, 1.

## SAYINGS OF THE GREAT

"When He who measures the duration of life has pronounced His decree, all the sciences of humanity are but useless essays."—*Napoleon I* (Contributed by F. C. Alton, O.B.E., F.R.C.S.).

"To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patience is never to go to sea at all."—*Osler.*

"Nothing's so hard but search will find it out."—*Herrick.*

"A wise physician, skilled our wounds to heal,
Is more than armies to the public weal."
—*Pope's translation of Homer's Iliad XI.*

# OBSERVATIONS ON THE APPEARANCES OF INTESTINAL TUMOURS

Lecture delivered at the Royal College of Surgeons of England

on

1st November, 1948

by

Cuthbert E. Dukes, O.B.E., M.D., Ch.B.,

Director of the Research Laboratory, St. Mark's Hospital

MUCH USEFUL INFORMATION can be gained by a good look at the outward appearance of an intestinal tumour. Of course microscopic examination is always necessary later on but few surgeons realise what a lot can be learned at once from a careful inspection of an operation specimen. The size, shape and colour of a tumour, its apparent extent of spread and the amount of free margin around are all details of surgical interest and may have significance in relation to prognosis. It must be admitted, however, that often these details are *not* observed because the operation specimen has been improperly treated and either mutilated by a surgeon or ruined by a pathologist! Both these should know that the best view of a tumour can only be obtained when the operation specimen has been pinned out or distended, then fixed and washed clean. A surgeon who slices open a tumour in the theatre "just to have a look at it" gets a poor view himself and obscures the view still more for others. Likewise a pathologist who plunges an operation specimen into formalin before taking steps to prevent shrinkage and distortion is making a mistake which cannot afterwards be rectified. Since so much depends on the initial treatment of an operation specimen let me begin with a description of the two methods which experience has led us to adopt as our routine at St. Mark's Hospital. One consists in stretching out the specimen on a frame: the other in distending it with formalin.

*The Stretching-Out Method* of preventing shrinkage is most suitable for comparatively short and straight pieces of bowel such as the distal end of the pelvic colon, rectum or anal canal. A large basin or sink must be available and rubber gloves should be worn. The operation specimen is first opened up with scissors taking care not to cut through the tumour if this can be avoided. The edges and ends of the bowel are then stitched with thin string to a framework of Meccano perforated strips (Fig. 1) after which the stretched-out operation specimen is immersed in a tall jar or tank containing 10 per cent. formalin and left there for a day or two. One advantage of the metal framework is that it keeps the specimen submerged. If it is pinned out on a cork mat or wooden board it must be sunk by attaching weights. Meccano perforated strips are a good investment for anyone who has much of this work to do.

*The Distension Method* is better for tumours of the small intestine and colon especially when these are to be preserved as museum specimens.

Fig 1. Operation specimen of Rectal Cancer stretched on frame for fixation.

The distal end of the bowel is ligatured and a glass tube is inserted into the proximal and secured in position with a slip knot. The intestine is then distended to natural size with 10 per cent. formalin run in under gravity from a bottle placed on a shelf. When full the operation specimen is pulled away from the glass tube, the noose being tightened at the same time to prevent the formalin solution from escaping (Figs. 2 and 3).

If an operation specimen cannot be dealt with immediately or if it has to be despatched elsewhere all that need be done is to wrap the entire organ in a damp cloth surrounding this with dry cotton wool and this again with a large towel or piece of jaconet. Kept in a cool place there will be no deterioration for a day or two. A few hours' delay before fixation is not injurious to an intact organ or large operation specimen though it may be ruinous to small pieces of tissue removed for biopsy; these should always be placed in formalin or other fixative immediately.

These methods of treating operation specimens have the advantage of displaying a tumour in its natural setting. The tumour becomes worth looking at: in fact, it seems to come to life! Moreover it becomes possible to observe fine points of distinction between benign and malignant tumours and between neoplastic and inflammatory lesions which otherwise might have been missed. Some of the more important features in the outward appearance of tumours will now be considered.

Fig. 2. Cancer of Hepatic Flexure, external view of distended specimen

Fig 3. Cancer of Hepatic Flexure, internal view of distended specimen.

## 1. BENIGN TUMOURS

A benign tumour seldom causes symptoms until it has assumed the shape and form of a polypus. The word polypus or polyp is a general term used to describe any pedunculated tumour whatever its nature. Most polypi prove to be inflammatory lesions or non-malignant tumours but an unsuspected focus of malignancy may sometimes be revealed by microscopic examination.

It is not difficult to explain why benign tumours tend to become polypoid whereas malignant ones do not. A benign tumour at first consists of a small well-defined nodule embedded in the bowel wall but as it increases in size it tends to project from the surface because there is more freedom for expansion in this direction. Gradually it becomes pedunculated owing to the pressure of peristaltic contractions and the traction exerted by the contents of the intestine. Malignant tumours on the other hand, even though they may at first project into the lumen of the bowel do not become extruded in this way because they are anchored to their site of origin by marginal infiltration into surrounding structures. It is useful to remember that a tendency to develop a polypoid shape is common to all types of benign tumours whereas for the most part malignant tumours tend to assume the form of ulcers.

(1) *Benign Epithelial Tumours.* Two varieties of benign epithelial tumour occur in the intestine, the adenoma and villous papilloma. Both arise from the glandular epithelium and as they grow each develops a distinctive appearance. An *adenoma* is at first a round firm sessile tumour, the surface of which is smooth or slightly nodular and the colour darker than the surrounding mucosa. As the tumour enlarges it develops a pedicle which gradually elongates until reaching even an inch or two in length. The stalk may be flattened from above downwards so that the tumour is suspended by a strap-like attachment (Fig. 4). If a pedunculated adenoma is cut open it will be seen that the stalk contains no tumour tissue but only a prolongation of the mucosa and submucosa containing blood vessels and connective tissues.

In contrast with this a *villous papilloma* is usually much larger. The growth has a characteristic convuluted appearance, more raised in the centre than at the margins which may be only slightly elevated above the surrounding mucous membrane (Fig. 5). Close inspection of the surface reveals a mass of delicate villi giving the tumour a velvety appearance. Villous papillomas are much less common than adenomas and rarely found elsewhere than in the rectum and pelvic colon.

The striking difference in gross characters of these two epithelial tumours is reflected also in their histology.

In villous papilloma the mucus secreting epithelium covers the outside of the central supporting core of connective tissue and blood vessels, the secretion being poured out on the surface whereas in an adenoma

the secreting cells are arranged as in tubular glands, mucus being discharged into a confined space. It would seem that a villous papilloma arises as the result of the proliferation of surface epithelium whereas an adenoma is the result of the neoplastic growth of epithelium in the depths of the intestinal crypts.

Fig. 4. Pedunculated adenoma of rectum.

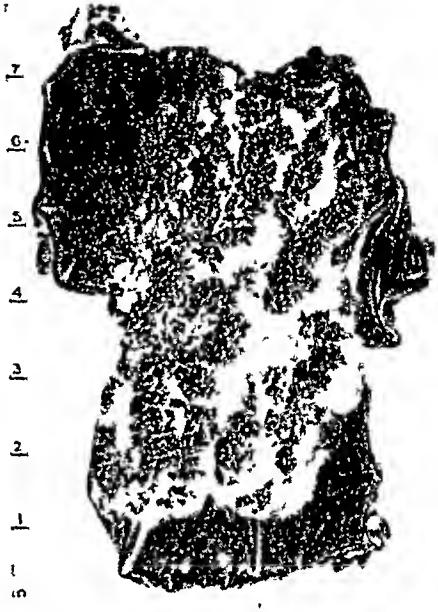


Fig 5. Villous papilloma of rectum removed by local excision.

Fig. 5.

The close relationship between benign epithelial tumours and malignant growths of the intestine is well known. As evidence the following points may be mentioned:

1. When patients with adenomas or papillomas of the rectum have been kept under observation over a period of years it has frequently been found that carcinoma has developed in a tumour previously known to be non-malignant.
2. It is not uncommon to find a small focus of carcinoma in a tumour, the greater part of which has the histology of an adenoma or villous papilloma. The carcinoma has developed in a pre-existing benign tumour.
3. Similarly at the edge of a frank carcinoma a careful search may reveal surviving portions of a benign tumour, the last remains of the forerunner of malignancy.
4. Familial polyposis is almost invariably followed by intestinal cancer and in this disease the first foci of malignancy are nearly always found in an adenoma or papilloma.

These facts justify the conclusion that an adenoma or papilloma should be regarded as a precancerous lesion. This does not mean that

all benign tumours inevitably become malignant or that carcinoma invariably begins in an adenoma or papilloma. These lesions are described as precancerous because cancer often develops within them.

The first indications of malignancy are darker colour and more solid consistence. Ulceration and induration of the base of a tumour are later and more certain signs of malignancy and when these are present the microscope seldom fails to confirm the clinical diagnosis of carcinoma.

(2) *Benign Connective Tissue Tumours.* These are rare, and only fibroma, myoma and lipoma need to be mentioned. *Fibromas* arise either from the loose connective tissue of the submucosa or from the sheaths of nerves. They develop into dense rounded encapsulated tumours which sooner or later become pedunculated. The cut surface shows a whorled appearance. *Myomas* resemble fibromas and can only be distinguished by microscopic examination. *Lipomas* may arise from either the submucous or subserous coats and appear as round polypi covered with intact mucosa. If the tumour is sliced open the interior is seen to be composed of adipose tissue.

(3) *Vascular and Lymphatic Tumours.* A massive *cavernous hæmangioma* may occur in the colon and give rise to persistent bleeding. It causes great thickening of the wall of the bowel which is dark and red through engorgement with blood. The lesion may extend over several inches of the colon and be accompanied by similar malformation in the blood vessels of the mesentery.

Tumours composed of lymphoid tissue may arise from the lymphoid follicles which lie in the submucosa. In its gross characters a *lymphoma* closely resembles an adenoma but it is easily distinguished by microscopic examination because it is composed entirely of lymphoid tissue with a layer of mucous membrane covering it.

## 2. LESIONS RESEMBLING BENIGN TUMOURS

The only lesions of the intestine likely to be mistaken for benign tumours are inflammatory polyps and cysts.

Any form of chronic ulceration in the intestine may be followed by so-called *inflammatory polyps.* They are met with most frequently after chronic ulcerative colitis or dysentery. If the polypi are scattered over a wide area the condition is described as pseudo-polyposis to distinguish it from true polyposis.

Inflammatory polyps differ from benign epithelial tumours in being more irregular in size and shape and in showing a more patchy distribution. Moreover the intervening mucosa is usually pale and atrophied and may show scars and furrows indicating healed ulceration. The polyps consist of tufts of granulation tissue and surviving tags of mucous membrane and if regenerative hyperplasia is in progress it may be difficult even by section to distinguish this from true adenoma. The distinction is important because inflammatory polyps do not tend to become malignant whereas adenomas do.

The secondary lesion of syphilis known as *condyloma* may bear some slight resemblance to a benign tumour when arising from the perianal skin. The syphilitic nature is proved by scratching the surface, collecting a drop of serum and examining for spirochætes by the dark ground test. The primary and tertiary lesions of syphilis are more likely to be mistaken for malignant tumours and will be referred to later.

Simple *anal warts*, non-specific in origin, have a rough fissured appearance. They are usually multiple and may surround the anus and extend into the anal canal. They are sometimes known as condylomata acuminata (meaning a protuberance covered with sharp points) but this term may lead to confusion with syphilitic condylomata. So anal warts is a better descriptive label.

The term *fibrous polyp* is used to describe hard pedunculated polypi arising in the ano-rectal region. They are derived most commonly from thrombosed hæmorrhoids but may arise also from hypertrophied anal papillæ. They consist of a central core of fibrous tissue covered by squamous epithelium and may protrude from the anus and resemble a neoplasm.

*Cysts* from the colon, rectum and perianal region are rare. Some are congenital in origin and others due to persistence of vestigeal structures. Also cysts may result from implantation by trauma or surgical operations.

(1) *Congenital Cysts.* When first formed the mucosa of the primitive large intestine is developed in longitudinal folds which are later replaced by villi. As development proceeds the villi disappear and the crypts of Lieberkühn are formed. During fœtal life cysts are often present in the bowel wall but they ultimately disappear by a process of degeneration.

A congenital cyst may occupy any part of the intestinal wall (intramuscular, submucosal or subserosal). In the colon a subserous cyst on the mesenteric border may lose its attachment and come to occupy a position between the layers of the mesentery at some distance from the bowel.

The term Colitis cystica is used to describe the presence of large numbers of cysts in the submucosa and mucous membrane of the colon.

(2) *Cysts derived from Vestigeal Structures.* Cysts between the rectum and sacrum have been attributed to the persistence of vestigeal structures such as the post-anal or tail gut and the neurenteric canal.

To understand these we must recall that when the hind gut is first enclosed the human embryo has no tail but this curious appendage is subsequently developed from the posterior extremity of the body of the embryo. Later a narrow tube appears within the tail communicating in front with the hind gut; this is the *post anal or tail gut.* It only exists for a few days, disappearing about the period when cartilage begins to be formed in the body and before the cloaca is divided into its rectal and genito-urinary portions. In mammals which normally possess

tails rudiments of the tail gut may be met with in any part of the tail. The anterior portion occasionally persists in man and maintains its connection with the rectum from which it extends backwards as a blind diverticulum.

The importance of the tail gut and neurenteric canal as an origin for cysts and fistulæ has been exaggerated. Most of the cases so described are more likely to have been dermoid cysts or teratoma.

(3) *Implantation Cysts.* Implantation or inclusion cysts originate from epithelium displaced by trauma or surgical operation. In the rectum they may give rise to lesions resembling sessile adenomata. On section a submucous implantation cyst appears as a cystic space filled with mucus and lined with mucus-secreting columnar epithelium. The histological diagnosis presents no difficulty if the possibility of such a lesion be kept in mind and if the fact of previous operation or injury is known.

## 3. APPEARANCES OF MALIGNANT TUMOURS

Malignant tumours of the intestine are nearly always unmistakably malignant in their appearance whatever their size or shape. None the less size and shape are important points to notice because they may have clinical significance especially in carcinoma. This is much the commonest variety of malignancy and will be considered first. The points of distinction between carcinoma and other rarer forms of malignancy will be dealt with later.

### CARCINOMA

For descriptive purposes we may distinguish six varieties of intestinal carcinoma, namely—malignant adenoma, malignant papilloma, protuberant carcinoma, ulcerating carcinoma, stenosing carcinoma and atypical carcinoma. This classification is based solely on gross characters but fits in well with other classifications based on histology and extent of spread.

The term *Malignant adenoma* is used to describe carcinoma arising in a pre-existing adenoma and *Malignant papilloma* a focus of carcinoma within a pre-existing villous papilloma. In both malignant adenoma and malignant papilloma the greater part of the tumour is benign and the carcinoma small and early. Malignancy results in a darker colour, local induration and ulceration.

The *protuberant type of carcinoma* differs from malignant papilloma in being malignant throughout. It projects into the lumen of the bowel causing partial obstruction (Fig. 6). Although the growth may be spread over a wide area on the surface there is often little penetration into the bowel wall. It is well known that protuberant varieties of carcinoma tend to remain localised and are slow to metastasise and in microscopic structure are often of a low grade of malignancy.

*Ulcerating carcinoma* is the commonest form of intestinal cancer. The ulcer may extend over two or three quadrants or completely encircle the bowel (annular growth). The edges are raised and everted and the

Fig. 6. Protuberant Carcinoma of pelvic colon.

outline serpigenous (Fig. 7). Depth of ulceration is usually proportional to extent of deep penetration. Small deeply ulcerated carcinomas often metastasise early and are of a high grade of malignancy.

The term *stenosing* (constricting or scirrhous) is applied to a carcinoma exceptionally dense and fibrous in character encircling the bowel and almost obliterating the lumen (Fig. 8). Intestinal obstruction is an early symptom with this variety of carcinoma.

The term *atypical carcinoma* is a convenient last resort. Most intestinal carcinomas fit in fairly easily into one or other of the five groups already mentioned but occasionally tumours are met with which have a very unusual and atypical appearance. For instance in some cases the primary tumour is exceptionally small or even apparently non-existent; in others the only lesion is a stricture or fistula. Atypical carcinoma is a useful pigeon-hole for hopeless misfits.

## SARCOMA AND MELANOMA

Other forms of malignancy such as intestinal sarcoma and melanoma are much rarer than carcinoma constituting less than one per cent. of malignant growths. In their earliest stages sarcomata form protuberant

Fig. 7. Ulcerating carcinoma of the rectum.

Fig. 8. Stenosing carcinoma of the pelvic colon.

Fig. 8.

growths covered with intact mucosa, but when they ulcerate they may be difficult to distinguish from carcinoma.

*Lymphosarcoma* is the commonest form of intestinal sarcoma. It may manifest itself either as a single localised tumour (Fig. 9) or give rise to a crop of tumours spread out over a long stretch of bowel. *Reticulum cell sarcoma* resembles lymphosarcoma in outward appearance and this too may assume a generalised form. It is a rarer tumour and has a worse prognosis. *Spindle cell sarcoma* generally appears as a bulky solid pedunculated tumour covered by intact mucosa (Fig. 10). *Melanomas* most commonly develop in the ano-rectal region and form dark tumours resembling thrombosed hæmorrhoids.

These rarer forms of malignancy can only be identified completely by detailed study of their histology but their outward appearance may make an experienced surgeon suspect that he is dealing with "something out of the ordinary." The differences in gross characters may be contrasted as follows:

| | CARCINOMA | SARCOMA | MELANOMA |
|---|---|---|---|
| Appearance .. | Most commonly an oval ulcerated tumour with raised margins. | At first a protuberant growth with intact mucosa. Ulcerated later. | Dark tumour resembling thrombosed hæmorrhoids. |
| Consistance .. | Feels solid and hard. | Rather soft Resembles brain tissue after fixation. | Firm, but not hard. |
| Cut surface (after formalin fixation) | Yellowish-white. | Greyish-white. | Light to dark brown. |

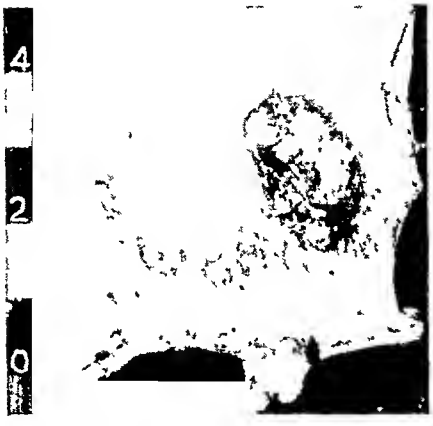


Fig 9. Lymphosarcoma of the rectum.

Fig. 10. Spindle cell sarcoma of the rectum.

*Carcinoid tumours* are fairly commonly met with in the appendix and are considered to be of a low grade of malignancy, very rarely giving rise to lymphatic metastases. Small nodules or plaques of carcinoid-like tumour tissue occur also in the rectum, but seldom grow to a sufficient size to cause symptoms. When developing in the small intcstine, however, carcinoid tumours are often invasive and metastasising growths. Most carcinoid tumours can be recognised by the characteristic yellow or orange colour of the cut surface.

Before leaving consideration of the gross characters of malignant tumours brief reference may be made to two additional points of surgical interest observable during the examination of an operation specimen, namely, the nature of adhesions and the significance of enlarged glands. *Adhesions* between the tumour-bearing segment of the bowel and other organs give the impression that the malignant disease has spread farther than may be the case. Such adhesions are much more commonly inflammatory than neoplastic in origin. Similarly the presence of *enlarged lymphatic glands* may suggest that the prognosis is worse than it is. Metastases certainly cause enlargement of lymphatic glands, but so does sepsis. In about half the cases in which the surgeon notices enlarged glands and comments on this the subsequent microscopic examination proves that the enlargement is due to sepsis and not to to metastases.

## 4. LESIONS RESEMBLING MALIGNANT TUMOURS

We began our description of malignant tumours by saying that they are " nearly always unmistakably malignant in their appearance " but it must now be added that many non-neoplastic lesions closely resemble malignant growths and are liable to be mistaken for them. In other words, a surgeon can nearly always recognise a malignant tumour for what it is but he may err in regarding a non-malignant lesion as a carcinoma or sarcoma.

Inflammatory and infective lesions if of large size, complicated by adhesions and accompanied by enlarged glands may be particularly difficult to distinguish from malignant growths. For instance, *pseudo-polyposis*, an example of which, following chronic ulcerative colitis, is illustrated in Fig. 11. Similarly in chronic *schisto-somiasis* the irritation caused by ova may result in the formation of papillomatous lesions resembling protuberant carcinoma (Fig. 12). Extreme *squamous cell metaplasia* of the rectal mucosa may also give rise to polypoid lesions closely resembling malignant papilloma.

Any form of intestinal ulceration may be mistaken for carcinoma especially ulceration caused by tuberculosis, syphilis and amœbic dysentery. *Tuberculous lesions* of the intestine vary greatly in appearance. The flat " girdle " ulcer bears little resemblance to a malignant growth but a tuberculous ulceration causing stricture in the ileo-cæcal region, or hyperplastic tuberculous lesions in the colon, or chronic tuberculous ulceration at the anal canal may closely resemble carcinoma. The case of generalised tuberculosis of the cæcum, ascending the transverse colon illustrated in Fig. 13 was diagnosed clinically as multiple malignancy.

*Secondary syphilitic lesions* such as condylomata have already been referred to. They are unlikely to be mistaken for a malignant tumour but chancre of the ano-rectal region may appear as a superficial ulcer with sharply defined borders and indurated base closely resembling epithelioma. Gummata of the rectum have been mistaken for carcinoma. This late manifestation of syphilis is rarely met with nowadays. At first it appears as an oval or round swelling in the submucosa, and when this breaks down and ulcerates, it may be difficult to distinguish from carcinoma.

Chronic ulceration due to *amœbic dysentery* has often given rise to errors in diagnosis and the resemblance to carcinoma may be very close (Fig. 14).

Naturally any obstructive lesion may be mistaken for a carcinoma. *Regional ileitis* for instance, is generally fairly easily recognised when limited to the distal end of the small intestine, but if it causes also a stricture in the colon, this may closely resemble carcinoma (Fig. 15). *Diverticulitis* has often been mistaken for carcinoma especially when it affects a short segment of the pelvic colon and leads to great thickening of the bowel and enlargement of the lymphatic glands owing to sepsis. Obstruction due to *foreign bodies* may lead to a mistaken diagnosis of carcinoma. A very unusual case of this sort is illustrated in Fig. 16. Three rabbit bones lying transversely had become impacted in the pelvic colon and caused inflammation and fibrosis leading to obstruction.

An obstructive lesion of the rectum and colon, difficult to distinguish from carcinoma, may be caused by *endometrioma*. The implants of endometrium first appear on the peritoneal surface and then begin to grow into the bowel from without inwards and in doing so cause a tumour which projects into the lumen of the bowel.

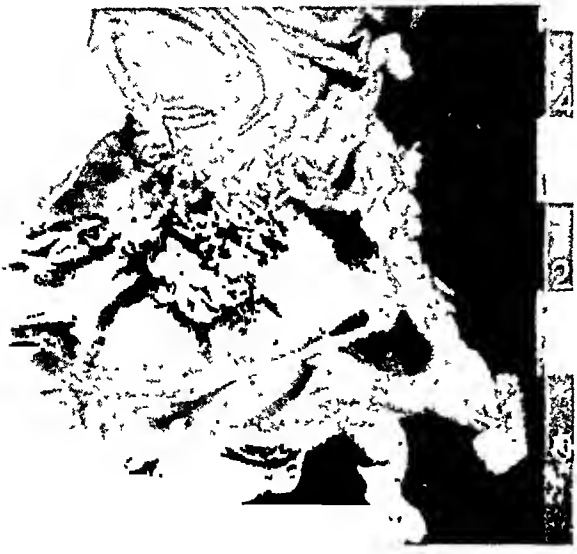


Fig. 11. Pseudopolyposis of cæcum resembling malignant papilloma.

Fig. 12. Schisto-somiasis of colon.

Fig. 12.

Fig. 13. Tuberculous lesions in colon resembling carcinoma.

Fig. 14. Amœboma of pelvic colon.

Fig. 14.

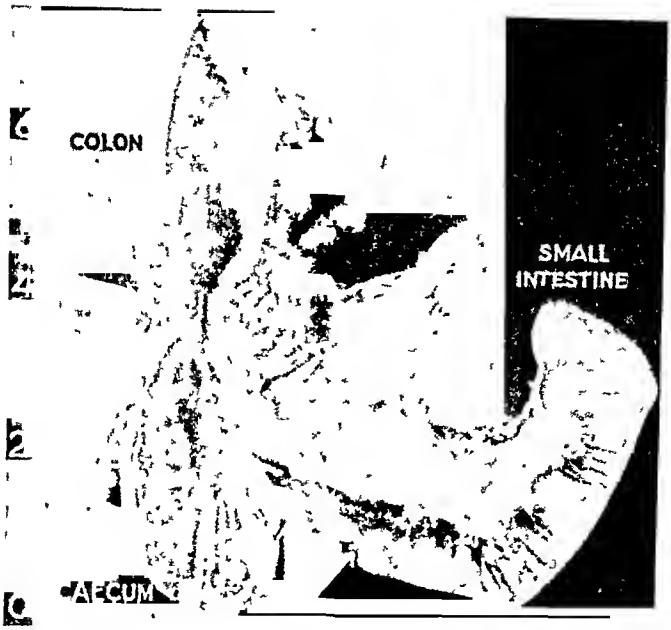



Fig. 15. Stricture of colon, associated with regional ileitis (stricture marked by arrows).

Fig. 16. Obstruction in pelvic colon caused by impacted rabbit bones.

Fig. 17. Endometrioma spreading from uterus to rectum.

This remains covered with intact mucosa for a long time though ultimately it may ulcerate. An example of endometrioma spreading to the rectum from the uterus and pouch of Douglas is shown in Fig. 17. This tumour had caused so much obstruction and kinking of the pelvic colon that perineo-abdominal excision and hysterectomy were necessary.

Various *malformations* may occur in the sacrococcygeal region resulting in swellings which may be mistaken for malignant tumours. *Dermoid cysts* of the sacrococcygeal region may result from inclusion of a portion of ectoderm during coalescence of cutaneous surfaces. These cysts may be either simple or complex in structure and are situated usually between the sacrum and rectum.

In infants *sacrococcygeal teratoma* may occur in the same region and they may be benign and cystic at first but often become malignant at an early age, developing into papillary adenocarcinoma. Mention must be made also of *chordoma*, a rare tumour arising in a remnant of the fœtal notochord. This may form an encapsulated tumour which may project either from in front or behind the sacrum.

Finally lesions resembling malignant tumours may occur in the rectum following the *injection treatment of hæmorrhoids* with non-absorbable oily solutions especially hydrocarbons of the methane series. These may give rise to nodular lesions in the submucosa of the lower third of the rectum followed later by stricture. If such a lesion is incised it is seen to have a yellowish hue and to be composed of a network of tiny spaces surrounded by fibrous tissue. The spaces may contain globules of oil which may be stained by fat stains. Strictures and tumours due to the injection of non-absorbable oils may resemble malignant tumours, but can easily be distinguished by biopsy.

I hope that what I have said has convinced you that it is worth while taking trouble to ensure that an operation specimen of a supposed intestinal tumour should be treated so as to provide a good view of the lesion in its natural setting. Also I hope I have convinced you that it is worth while for a young surgeon to train his eye to notice fine points of distinction in the external appearance of intestinal tumours and to correlate these with the information subsequently to be derived from the microscope.

---

*NOTE.*—A second article entitled "The Significance of the Unusual in the Pathology of Intestinal Tumours" will appear in the next issue of the ANNALS.

# MALIGNANT DISEASE OF THE PARANASAL SINUSES

Lecture delivered at the Royal College of Surgeons of England

on

2nd May, 1947

by

F. C. W. Capps, L.R.C.P., F.R.C.S.
Surgical Throat and Ear Department, St. Bartholomew's Hospital

IT WOULD SEEM to be fairly generally accepted that primary malignant disease occurs only in the maxillary antrum or ethmoid cells. By the time it is recognised, however, it has usually extended far beyond the site of origin and the latter is in the vast majority of cases uncertain.

Histologically and clinically it is convenient to group together all those cases of tumour which involve either a sinus alone, the upper jaw generally, or the nasal passage behind the vestibule and anterior to the posterior choana. It is true that this may include growths primary on, or deep to, the mucous membrane of the septum, but these are rare compared to other sites of origin in the nasal passage and in any case spread ultimately to the regions with which we are concerned and may be said to affect them secondarily.

By this grouping we exclude all tumours arising in the post-nasal space, the oral surface of the palate and the vestibule or external coverings of the nose, all of which clinically, and to some extent histologically, fall into very different groups.

St. Clair Thomson and Negus in their book, state that malignant growths are met within this region (nose and accessory sinuses) with moderate frequency and that it is well to remember that they are more common than simple neoplasms. If we accept the fact that simple mucous polypi are not new growths, this is certainly true.

Ewing(1), in a review of a large number of malignant tumours of all types found that 1·84 per cent. occurred in the maxillary antrum.

Most authorities seem now to agree that the commonest tumour in this region is a squamous-celled carcinoma of varying degrees of differentiation.

G. B. New(2), in a review of 295 cases in 1938 states that the squamous-celled form a much higher proportion than formerly and attributes this to a change in the viewpoint of the pathologists.

Harmer(3), in his Semon Lecture (1931) states that in his opinion the commonest growth is definitely a squamous-celled type.

Windeyer(4), in his Skinner Lecture (1943) reviewed the histology of 75 cases of carcinoma in which the specimens were intact and found a high proportion of squamous-celled and transitional.

Öhngren(5) divided 149 cases into 116 epithelial, 22 connective tissue, and 11 malignant mixed tumours. I give you also a survey of 51 cases of my own from 1929 to 1947.

**NEW**

| | |
|---|---|
| PRIMARY TUMOURS: | |
| Squamous-celled | 63 |
| Adenocarcinoma | 6 |
| Round-celled sarcoma | 7 |
| Myxo sarcoma | 1 |
| Fibro and Osteo sarcoma | 9 |
| Lympho sarcoma | 3 |
| Malignant, but type of cell not determined | 2 |
| | 91 |
| SECONDARY TUMOURS: | |
| Squamous-celled | 30 |
| Adenocarcinoma | 5 |
| Round-celled sarcoma | 1 |
| Myxo sarcoma | 1 |
| Fibro sarcoma | 2 |
| Malignant, but type of cell not determined | 11 |
| | 50 |

**CAPPS**

| | |
|---|---|
| Squamous-celled | 24 |
| Adenocarcinoma | 7 |
| Lympho sarcoma | 3 |
| Osteoid sarcoma | 1 |
| Myelana | 1 |
| Hæmangeio endothelioma | 3 |
| Malignant, but type of cell not determined | 12 |
| | 51 |

**ÖHNGREN**

| | |
|---|---|
| EPITHELIAL: | |
| Squamous-celled with hornifications | 58 |
| Squamous-celled without hornifications | 40 |
| Transitional-celled | 4 |
| Basal-celled | 5 |
| Undifferentiated | 9 |
| | 116 |
| CONN. TISSUE: | |
| Spindle-celled sarcoma | 2 |
| Round-celled sarcoma | 3 |
| Polymorphous-celled sarcoma | 3 |
| Melano sarcoma | 3 |
| Osteoblastic sarcoma | 5 |
| Myxo sarcoma | 2 |
| Fibro sarcoma | 1 |
| Plasmacyto sarcoma | 3 |
| Mixed salivary gland tumours | 11 |
| | 33 |

**WINDEYER**

| | |
|---|---|
| Keratinising squamous-celled | 22 |
| Little keratinisation | 23 |
| Transitional | 18 |
| Undifferentiated spher. celled carcinoma | 9 |
| Adenocarcinoma | 3 |
| | 75 |

Ewing also describes papillary carcinoma, basal-celled carcinoma (adenocystic endothelioma or cylindroma), cylindrical adenocarcinoma, round-celled carcinoma (often called sarcoma) and dental tumours (squamous and glandular adamantinomas). Squamous-celled carcinoma, he considers, arises from metaplasia of previously altered lining epithelium.

New also reports melano-epitheliomas, hæmangeio-endotheliomas and multiple myelomas. Several of those in my small list represent carefully revised opinions where the report and appearance were equivocal. In the last 12 the histological reports were regrettably absent, and the disorganization of war has not yet permitted a hunt for sections

or a search of the records in the Pathological Department. One has since been found and shows a cavernous angeioma.

The incidence is usually said to be higher in males than in females. In Ballenger's textbook the ratio is said to be as high as 7 : 1. Öhngren(5) in 187 cases gives 101 males to 86 females. Windeyer(4) in 153 cases, 81 males to 72 females. My own 51 were 23 males to 28 females. There may be nothing in the sex incidence or, possibly, like some other neoplasms it is now becoming more common in women.

The age incidence rises rather sharply after the age of 40 to a maximum between 50 and 70, and then falls again. This corresponds with the age incidence of most other malignant tumours.

Carcinoma is usually a disease of adult, and rather advanced adult age. Sarcoma is often found in younger persons.

Nothing is known of the ætiology. In a few of Windeyer's cases there was a history of long-standing sinus infection with multiple operations for removal of polypi. There were two such cases in my series.

Clinically, owing to their diffusion, it is difficult to classify the tumours. Three criteria of Öhngren(5) seem most apt :

1. The more or less favourable position of the tumour.
2. The greater or lesser degree of histological malignancy.
3. The presence or absence of metastasis.

He also divided them by a plane from the inner canthus of the eye to the angle of the jaw into antero-inferior and postero-superior groups, and further, by a line perpendicularly through the pupil, each main group could be divided into medial and lateral. The degree of malignancy ranges from lowest in the antero-inferior medial through antero-inferior lateral and postero-superior lateral to highest in the postero-superior medial group.

Patterson(6) simplifies this somewhat. He imagines a horizontal plane through the roof of the antrum and a vertical plane corresponding to its posterior wall. Growths above the former and behind the latter are relatively unfavourable.

New(2) would add age, general condition and *ability to return for observation.* Commenting on this classification New(2) says : " It is readily seen that as compared with postero-superior tumours those which are antero-inferior are much more easily removable and they may become of large size without invading regions that make their removal impossible."

Opinions differ as to early or late metastasis in glands or distant areas. Harmer(3) states that it is late. New holds it to be early. Butlin(7) said " The rule, however, is that the tumours of the antrum either do not affect the glands or only do so when the disease is very advanced." Windeyer found glandular metastasis in 32.7 per cent. of 153 cases, and generalised metastasis in 9 per cent. In four cases in my series glands in the tonsillar or submaxillary region were noted when first seen, three of them squamous-

celled carcinoma, and in another squamous-celled submaxillary glands developed later.

*Symptoms.* Early symptoms are absent, and Butlin's(7) classical description of the symptomatology cannot be bettered to-day. " Sometimes the appearance of the tumour is preceded by pain, but in many instances there is no pain until the disease is advanced. The first sign of serious disease is the appearance of a swelling of the face over the antrum or of fullness and obstruction of the corresponding side of the nose. With the fullness of the nostril there may be discharge of bloody fluid. The swelling gradually increases, not only in the directions in which it was first noticed, but also up towards the orbit, down towards the mouth, and back into the sphenomaxillary fossa. The eye may be pushed up and the hard palate pushed down, but the swelling in the fossa is not so easily perceived. The nostril on the affected side often becomes completely obstructed. As the disease advances, the bony wall may be destroyed and protrusion may take place, with affection of the soft parts around the bone. The skin of the face in this way becomes adherent to the tumour and immovable over it, and the result may be a vast ulcer, with the thrusting forth of a fungous mass." (See Fig. 1.)

By kind permission of The Medical College, St. Bartholomew's Hospital

Fig. 1A. Before treatment. Swelling of right cheek. Right nasal obstruction. Swelling of right side of palate.

Fig. 1B. Six months after treatment by million volt deep X-ray. Clear airway. No swelling of cheek Slight residual swelling of palate. Clinically and by X-ray no evidence of growth and as patient 80 years old operation not contemplated.

He does not mention epiphora which has been an early symptom in a sufficient number of cases to stress the fact and draw to it the attention of our ophthalmological colleagues.

Where accurately recorded I found that the first symptoms complained of in my cases were:

| | |
|---|---|
| Polypus or nasal obstruction | 20 |
| Swelling of cheek, palate, or displacement of the eye and broadening of the nose | 20 |
| Pain | 9 |
| Bleeding or discharge, or both | 9 |
| Epiphora | 3 |
| Diplopia | 1 |
| Swelling as a result of injury | 2 |

Of the obstruction there is nothing much to say. Absolute obstruction of a nasal passage due to new formation is almost pathognomonic of malignancy. Simple polypi rarely cause complete stoppage of ingress and egress.

Rapidly increasing obstruction, especially unilateral, and in the elderly and up to then freely breathing subject, calls for most thorough investigation.

Of swelling of the cheek New(2) says, significantly, that if it is not due to an obvious inflammatory condition of dental origin, it is very suspicious. He states, what I have always taught, that except in osteomyelitis, inflammatory conditions of the antrum do not cause bulging of the cheek. Pain is described as dull and persistent, worse on lying down and may be associated with areas of paræsthesia or anæsthesia of the cheek. It is frequently referred to the teeth and numbers of cases come first into the hands of dental surgeons, and not a few have had extractions. Sometimes the socket fails to close and there is a fetid discharge.

A unilateral offensive discharge if not due to a foreign body or anærobic infection of the antrum must be regarded with suspicion and repeated unilateral epistaxis or ready bleeding on examination in the elderly, should put one on guard.

Concerning epiphora, Öhngren(8) suggests X-ray of the tear ducts and sac after the injection of lipiodol. Although they may apparently be patent this may show deformity due to the pressure of a tumour. Teeth may loosen and fall out painlessly.

## DIAGNOSIS

Under symptomatology we have pointed out many of the factors which would lead to a clinical diagnosis. X-rays may help considerably. A malignant growth usually gives a very dense shadow, usually ill-defined, and in the advanced cases (and unfortunately as has been said before, many are far advanced before they seek opinion) there may be obvious destruction of the bony walls of the nasal passage or maxillary antrum. (See Figs. 2 and 3.)

Fig. 2. Shows erosion of posterior wall of Rt. antrum and invasion of pterygo-maxillary fossa.

Fig. 3. Shows erosion of orbital margin and outer wall of Lt. antrum.

Lastly, there is the histology, and on this several points.

It has been pointed out by all workers that it is important to get a specimen from deep in the growth. The surface may be covered with polypoid and non-invaded mucosa, or there may be such necrosis or secondary infection that a misleading or equivocal report is received. In the highly malignant types of growth the risk of lymphatic dissemination by the trauma of examination or biopsy must be taken seriously. Öhngren and others advocate the removal of the specimen by diathermy. I have quite frequently resorted to three preliminary irradiations as a safeguard. New holds the correct procedure to be a frozen section and immediate radical endothermic surgery if the diagnosis is proven.

The differential diagnosis must be made from syphilis (Öhngren insists on the importance of Wasserman or a similar serological test on all patients), tubercle, innocent growths, foreign bodies, rhinoscleroma and Boeck's sarcoidosis.

## TREATMENT

Pure surgery is now a thing of the past, though it is amazing to record that Butlin, by local excision or resection of the upper jaw, without the aid of diathermy, transfusion or chemotherapy, achieved two three-year and three over three-year cures in 14 cases. The operative mortality was, at the time, very high, chiefly from loss of blood and chest complications. It was about 30 per cent. of 74 cases in the Gottingen Klinik between 1875-96. Nowadays the operative mortality for these growths is small.

In 28 operations, other than biopsy, performed in my 51 cases, only one died four days after operation for advanced disease. For the great improvement in operative and post-operative mortality we must pay tribute to improved anæsthesia, chemotherapy and transfusion.

Any surgical procedure in these days should be performed by diathermic cutting and coagulation, unless a lateral rhinotomy through unaffected skin is being performed. Resection of the jaw as such is unnecessary. It often removes much that is healthy and fails to reach extensions to the orbit, pterygo-maxillary fossa, post-nasal space and sphenoid. Diathermy through a proper approach can chase the growth wherever it goes. Personally, I have found a sublabial approach to nasal passage and canine fossa (Denkers) to be adequate for the vast majority, but others prefer wider access, particularly for growths lying high up and far back. There is a definite advantage, if there is no involvement, in leaving as much of the palate as possible, as it makes the patient's feeding and speech a much more comfortable matter. Even if in cases of doubt, one diathermies the floor of the antrum with subsequent sequestration of the bone and sloughing of the soft tissues, the initial stages are still rendered much more comfortable. Harmer, however, always advocates removal of half the hard palate. Removal through the nostril alone must always be considered inadequate and unsafe.

With diathermy you can go right to the base of the skull and the risk of sepsis and hæmorrhage is much less than by surgery, while your coagulation goes considerably deeper than its visible extent, a matter of some importance where a very free lymphatic drainage is involved. If the orbit has been invaded it should be exenterated. New says: "The loss of an eye or perforation of a cheek are of secondary importance; plastic surgery can repair the deformity." Though not, of course, the sight of an eye, and where there is reasonable doubt it may be justifiable to remove the orbital plate, diathermy the periglobar tissue and hope for the best.

Ligature of the external carotid is done by some and regarded as quite unnecessary by others. It certainly will not stop secondary hæmorrhage, but I believe it does reduce hæmorrhage at the operation if done at the same time and so shortens the time taken. It does also give a chance of removing a lymph gland for histology.

Deep X-ray, teleradium, and interstitial radium, and radon are all employed, also post-operative intracavitary radium. In seven cases in my series complete regression of the primary tumour was achieved by radiation alone.

1 well differentiated squamous cell.
1 carcinoma (type not recorded).
1 lymphosarcoma.
1 myeloma.
2 hæmangeioendotheliomata.
6

Four are alive and well. The lymphosarcoma had a recurrence in ribs the same year, treated by further radiation, a recurrence in the lower ileum two years later excised and irradiated, and died 11 years after she was first seen from multiple secondaries, aged 23. One hæmangeioendothelioma had three courses of deep X-ray, but died 13 years later, aged 25. The remainder are alive and well.

As a rule radiation by itself is inadequate; growth is nearly always found at operation even after a very full dose. A combination of radiation and electro-surgery seems to give the highest proportion of successes, and the only difference of opinion seems now to be whether to irradiate before, after, or before and after operation.

If irradiation is done first then it is essential to wait for the skin reaction to subside before operation. Personally, I prefer irradiation by deep X-ray (I have never had access to a radium bomb for these cases) followed by diathermy exenteration and, if necessary, intracavitary radium (applied by the now accepted method on the surface of a mould made to fit the cavity, not inserted in the middle of a pack).

I believe the periphery is thus shut off and the growth reduced to more manageable proportions, but others argue that one may thereby miss areas involved but not obvious when one operates and prefer to destroy all macroscopic growth by operation and rely on subsequent irradiation to exterminate the microscopic. It is a matter of choice. Where extensive skin incisions are planned there may be a risk of delayed healing if irradiated before operation. Post-operative irradiation after healing may be better in these. Irradiation in the presence of gross sepsis is dangerous, and either a drainage operation or primary operative exenteration is desirable. With regard to the glands of the neck some still do block dissections, but I think the majority rely on irradiation. In any case the first glands in the chain of lymphatic spread are the unapproachable retropharyngeal group.

## RESULTS AND PROGNOSIS

Both of these have improved very greatly in the last two or three decades. New(2) goes as far as to say that in the last 15 years there has been no greater advance in the treatment of malignant tumours than in that of the upper jaw. Operative mortality is much reduced and more patients are alive without recurrence. Increasingly expert anæsthesia, pre- and post-operative chemotherapy and transfusion, in all its aspects, have contributed greatly to the first of these.

They would be even better, how familiar it sounds, if only an earlier diagnosis were possible. Öhngren(8) says: "The value of increased knowledge among the general public would be that the patients would go to a doctor of their own accord, before the tumour has spread to the extent that is now usual. In general malignant tumours are now met with in the latter decades of human life, and, therefore, patients who

have previously been healthy, but begin to be troubled by pain in the trigeminal area, by one-sided obstruction of the nose, by nose bleeding, or by purulent secretion from the nose, should be subjected to more frequent X-ray examination, exploration of the antrum from the canine fossa, and biopsies from the nasal cavity. The instinctive attitude of the doctor that, as a matter of course, he does not lose sight of older patients suffering from these symptoms until he has carried his investigations so far that he can either exclude the possibility of a tumour or definitely prove the existence of one, would in many cases render possible a sure diagnosis months earlier than is the case at present."

New(2) has noted that extensive, primary, highly malignant tumours often give better results than those of the same size, but low-grade malignancy. The reason is that radiation treatment will destroy the highly active ones, whereas every particle of a tumour of low grade must be removed by diathermy, and this is no easy matter.

Some one in 10 cases will lose an eye, either by deliberate design or from subsequent ophthalmitis.

Of 295 cases in which operation was performed before 1929 in the Mayo Clinic, 236 were traced and 127 or 53·8 per cent. were without recurrence five years later. Of apparently primary tumours (of the antrum) 75 out of 91 were traced and 30 or 40 per cent. were without recurrence after five years. Of secondary antral tumours, 43 out of 50 were traced and 23 or 53·4 per cent. were without recurrence after five years. Of upper jaw and palate cases 118 out of 154 operations were traced and 74 or 62·7 per cent. were without recurrence five years later. In all these there is a fairly high percentage of the untraced, which make the percentage of successes look a little optimistic.

Öhngren(5) records 235 cases in which operation was performed between 1924 and 1936, and gave the end-results in 120 cases in which it had been possible to follow the patients for five years or more. Of these 42, or 35 per cent., were alive and well 5-12 years after treatment (cf. Mayo Clinic, 53·8 per cent. Öhngren had a very small proportion of untraced cases).

Windeyer and Wilson, who traced 97 per cent. of their cases, had 18·8 per cent. five-year success in 69 cases treated between 1925 and 1935, and 30·8 per cent. five-year success in 13 cases treated in 1936 and 1937. Up to 1943 his percentage of three-year successes was rising in spite of the fact that all cases, however advanced, were being treated. Of nine cases of sarcoma treated prior to 1937, only one, a fibrosarcoma of relatively low malignancy survived symptom-free for five years.

In 37 of my 51 cases, which have been observed for five years or more after treatment, 14 were symptom-free for 5-18 years. Two only in this period were untraced, and all cases were treated. This gives 37·8 per cent., and includes in a much smaller series than the others three cases at least of low-grade malignancy. Of cases classed as carcinoma (of all

types) 10 out of 17 were symptom-free for five or more years. The sarcomata were bad as in Windeyer's series; one out of four only being alive and symptom-free for 15 years, and that an osteosarcoma. The other three were lymphosarcomas, and two died while still under treatment, and the third, after having recurrences within a year and two years successfully treated, died of numerous secondaries after nine years of freedom. Hæmangeio endothelioma also seems liable to long-term malignancy. Of two cases, both of which were treated by irradiation only, and required more than one course or type of radiation to control, one died of recurrent disease after being free for 13 years. Lastly, we must say that for success, very devoted after-care is necessary. Crusting and sequestra need constant attention, and the control of pain and maintenance of the patient's morale is of vital importance.

With regard to any subsequent deformities or deficiencies it seems to be generally accepted that cheek, nose, eye socket, etc., are best closed by plastic flaps, but the palatal deficiencies are much better repaired by dental obturators, which it is now possible to make extremely light and which can carry teeth.

Harmer([3]), in his very thorough review of the situation in 1931, recorded 819 cases from many sources and many types of treatment; 427 were dead—136 were lost—207 were alive without disease—63 for five years or over, and 49 were alive with disease. The comparable figure to the other series is 63 symptom-free for five or more years, in 683 cases only about 9 per cent. Perhaps the value of many small series added together with bigger series gives a false picture. The value of team-work emphasised by Windeyer is outstanding, and cases are probably better concentrated into a few well-equipped centres.

## REFERENCES


1 EWING, J. (1940) *Neoplastic Diseases*, 4th edition, p. 782.

2 NEW, G. B. (1938) *Amer. J. Surg.* **42**, 170; (1946) Jackson *Diseases of the Nose, Throat and Ear*, p. 72.

3 HARMER, W. D. (1931) *The Relative Value of Radiotherapy in the Treatment of Cancers of the Upper Air Passages.* Semon Lecture.

4 WINDEYER, B. W. (1943 and 1944). Malignant Tumours of the Upper Jaw. *Brit. J. Radiol* **16**, 362; **17**, 18.

5 ÖHNGREN, L. G. (1933) *Acta Otolaryngologica Supplement* **19**.

6 PATTERSON, N. (1937) *Journal of Laryngology & Otology* **52**, 38.

7 BUTLIN, H. T. (1900) *The Operative Surgery of Malignant Diseases*, 2nd edition.

8 ÖHNGREN, L. G. (1937) *Journal of Laryngology & Otology* **52**, 26.

# OSTEOMYELITIS OF THE MANDIBLE

Based on a lecture delivered at the Royal College of Surgeons of England

on

19th February, 1948

by

S. H. Wass, M.S., F.R.C.S.

Assistant Surgeon to Guy's Hospital

THE COMMONEST CAUSE of osteomyelitis of the mandible is dental infection, an extension of apical or peri-apical disease resulting in spreading inflammation of bone. Osteomyelitis also follows infected fractures of the mandible and occasionally complicates infected cysts. It can occur from a blood-stream infection, particularly in infants or young children, and rarely from metastatic invasion of the mandible in a patient suffering from acute osteomyelitis of another bone. Cases of osteomyelitis of the mandible arising by direct extension from a staphylococcal boil on the chin have also been recorded. Dental infection, however, is by far the most important cause and my further remarks will be confined to this type of the disease.

## OSTEOMYELITIS OF DENTAL ORIGIN

There has been a great increase in the incidence of osteomyelitis of dental origin since the early years of the war. Statistical evidence in support of this statement is difficult to obtain but the following figures illustrate my own experience with the disease. In the 10-year period 1933-1942, 51 patients were admitted to the wards of Guy's Hospital suffering from osteomyelitis of the mandible. This is an average of 5·1 patients per year under the care of all the surgeons and dental surgeons together, less than one per year for each surgeon. In the succeeding five years, 1943-1947, I treated 57 patients myself, an average of 11·4 patients per year for a single surgeon; and in 51 of these 57 patients the osteomyelitis was due to dental infection. In other words, I have had the opportunity of treating personally more patients with osteomyelitis of the mandible in the last five years than were treated by the whole staff of Guy's Hospital during the preceding 10 years. One cannot fail to be impressed by these figures and the experience of other surgeons confirms my belief in the absolute increase in the incidence of dental osteomyelitis. It behoves us, therefore, to study the factors which cause the development of osteomyelitis, ponder upon its increasing frequency, and consider what steps can be taken to prevent it.

### Ætiology

Osteomyelitis of dental origin almost invariably arises from apical or peri-apical disease. Apical infection in relation to a live tooth causes symptoms which are easily recognised. If these symptoms are ignored, or do not become apparent because the tooth is dead, the apical infection may spread *through* the bone to produce a cellulitis of the soft tissues

or an alveolar abscess. This is the commonest acute infection of the jaw and must not be confused with osteomyelitis ; primary soft-tissue infection is seldom followed by bony disease, even in neglected cases. In only three of my 51 patients has osteomyelitis followed a primary alveolar abscess. It is a mystery why such spreading infection so commonly reaches the soft tissues without producing bony disease but it is a fortunate happening, for otherwise osteomyelitis of the jaw would be the scourge of humanity.

In some cases, however, spreading peri-apical infection *does* involve the bone of the jaw and osteomyelitis becomes established. Can we explain why this happens in only the minority of cases ? Bone is a tissue normally resistant to the spread of apical disease ; osteomyelitis will only develop if the infecting organism is of a particular variety or virulence, or if there is lowering of the general resistance of the patient or local resistance of the bone.

The common organism causing osteomyelitis of the mandible is the staphylococcus aureus, but in the jaw it is seldom highly virulent. Even the most severe cases of dental osteomyelitis are not complicated by septicæmia or pyæmia and do not show the degree of constitutional disturbance which is present in acute osteomyelitis of the long bones. It cannot be assumed, therefore that the development of osteomyelitis of the mandible is due to the virulence of the infecting organism alone ; and the mere presence of the staphylococcus aureus in an apical area does not necessarily mean that bony disease will occur. The organism may lie dormant, showing no tendency to invade the bone ; and when it does cause spreading inflammation a simple alveolar abscess results more commonly than osteomyelitis.

As in all infections, therefore, the onset of osteomyelitis must be determined by the outcome of the battle between the pathogenic organisms and the general and local resistance of the tissues of the host. General resistance to infection is a term impossible to define, depending as it does upon natural and acquired immunity and all the factors which affect such immunity. It is known that severe anæmia, and other blood diseases such as leukæmia, are associated with diminished resistance to infection, particularly within the buccal cavity ; but in my series of 51 patients with dental osteomyelitis there has been no example of severe blood disease. Minor degrees of anæmia, however, have been common and they also may be associated with lowered resistance. Experience in other fields has led me to believe that the war-time dietary has produced a diminished resistance to pyogenic infection. The increase in the number of cases of osteomyelitis of the mandible has only been apparent since about 1942 and I feel convinced that a state of subclinical under-nutrition, the result of prolonged restrictions of diet, is an important factor in accounting for an otherwise inexplicable increase in the incidence of this disease.

The factors affecting local resistance within the bone of the jaw are equally difficult to study with scientific accuracy. Infection around a buried root

or dead tooth may be complicated by the development of a chronic form of osteomyelitis, even after a lapse of many years. On other occasions, however, buried roots or dead teeth cause no trouble ; and osteomyelitis is known to occur from infection of live teeth. It is unconvincing, therefore, to assert that buried roots or dead teeth act as so-called " irritants " which diminish local resistance to infection.

Mowlem (1944) has pointed out that the mandible shows an anatomical feature predisposing to the spread of infection and accounting for the frequent occurence of osteomyelitis in the lower jaw compared with its relative rarity in the upper jaw. Apart from small arteries from the periosteum, the mandible derives its entire blood supply from a single artery running horizontally in a bony canal. The maxilla, on the other hand, is supplied by a series of vertically disposed segmental arteries. It follows, therefore, that infection and inflammatory exudate in the mandibular canal may cause thrombosis of the main artery, thus cutting off the entire blood supply of the bone and preventing the development of a defensive inflammatory reaction. In the maxilla, with its multiple arteries of supply, collateral circulation is free and resistance of the bone to spreading infection is not so hampered by vascular thrombosis. These anatomical features undoubtedly affect the relative incidence of osteomyelitis in the upper and lower jaws, but they do not account for the increased number of cases of osteomyelitis of the mandible in recent years.

Before leaving the question of local resistance to infection the relation between dental extractions and the development of osteomyelitis must be discussed. In my series of 51 cases of osteomyelitis of dental origin, two-thirds, or 34 cases, followed dental extraction. Of these 34 post-extraction cases, 18, or over 50 per cent., showed evidence that the dental treatment leading up to the development of the disease had been of poor quality. Whilst good dentistry may be followed by osteomyelitis, bad dentistry, in my opinion, is an important factor in diminishing local resistance and increasing the likelihood of onset of the disease. The following typical history of a patient with osteomyelitis bears out this contention. The patient complains of throbbing toothache, clearly indicating the presence of an apical abscess, yet local submucous analgesia is employed. The extraction itself is unskilful and is accompanied by breaking of crown or roots. The operator, under the same local analgesic, then causes further injury by using elevators to complete the extraction. Pain and swelling of the jaw follow this treatment and adjacent teeth are removed in the mistaken belief that they are responsible for the symptoms. This story is no exaggeration, it occurs time and again. The danger of local analgesia in the presence of sepsis is well known. Traumatic extractions of the type described *must* tend to cause vascular thrombosis and lead to the spread of infection. Pain and swelling after extraction should be a warning that osteomyelitis may have developed and in the presence of bone infection further extractions, even of loose teeth, should

*not* be performed until attention has been directed to the bony disease itself. Yet one or more of these basic principles was ignored in 18 of my 34 patients with post-extraction osteomyelitis.

## DIAGNOSIS

There are two main clinical varieties of osteomyelitis of the mandible. One can be called diffuse or spreading osteomyelitis, the other chronic localised osteomyelitis.

(1) *Diffuse or spreading osteomyelitis* is usually considered to be "acute," but the use of this adjective is misleading. As already pointed out, osteomyelitis of the mandible, even in its most severe form, is not comparable with acute osteomyelitis of a long bone. It is not complicated by septicæmia or pyæmia and is not accompanied by high fever or serious constitutional disturbance. It is a subacute disease with low fever and only a mild degree of toxæmia.

The majority of cases follow dental extraction. My series includes 33 examples of this subacute type and 25 of them followed extraction of teeth. The remainder occurred without any extraction taking place or had symptoms suggestive of osteomyelitis before dental treatment was given. Most cases in which no extraction had been performed showed evidence of a dead tooth at the site of infection. The disease affects the two sexes equally and occurs at all ages, though rare in children. My youngest patient was 16 years of age, my oldest 60, and two-thirds of the patients belonged to the 20-40 age group.

The symptoms cause attention to be sought early, but from three weeks to two months is the common duration of symptoms before a diagnosis is made. *Pain* and *swelling* are constant features and trismus is present if the disease affects the molar region or ascending ramus of the jaw. *Pain* may be severe and is of the constant boring type characteristic of bony inflammation. Evidence of involvement of the inferior dental nerve is forthcoming when pain is referred to the ear or numbness occurs in the mental region. The *swelling* is of two types. In some cases there is swelling of the bone with minimal œdema of the soft tissues. This swelling is due to periosteal thickening or the formation of subperiosteal granulation tissue or new bone, and is associated with tenderness in the affected region of the jaw. In other cases bony swelling is masked by gross œdema of the soft tissues due to secondary cellulitis, and abscess formation may take place in neglected cases. This variety is difficult to distinguish from a simple alveolar abscess unless there is radiographic evidence of bone disease, and in my experience it carries a worse prognosis than that in which the soft tissues remain relatively unaffected. There is often a *purulent discharge* into the mouth, through a tooth socket or secondary sinus, and the occurrence of this discharge may be associated with disappearance of pain due to relief of tension within the bone.

*Radiographic confirmation* of the diagnosis is not forthcoming in the early stages of the disease, an important point to remember. The first

radiographic sign is loss of bony detail, giving a mottled or moth-eaten appearance, often only appreciated when compared with normal radiographs taken at an earlier stage of the disease. The area of bone destruction gradually becomes more extensive but even at relatively late stages sequestration may not be evident radiographically; small sequestra are frequently masked by the density of the cortical bone of the jaw. In some late cases, however, dense sequestra are visible and a pathological fracture may be seen. The earliest radiographic evidence of bone destruction seldom appears until bone infection has been in progress for three weeks. A clinical diagnosis of osteomyelitis may be possible earlier than this when bony swelling is present, but when soft tissue swelling predominates it is difficult, if not impossible, to distinguish between osteomyelitis and alveolar abscess in the first three weeks. If incision of a soft tissue abscess is followed by disappearance of all symptoms and signs, osteomyelitis is not present. Some alveolar abscesses, however, pursue a relatively chronic course and suppuration is slow to take place; in such cases it is only if good radiographs show no bony disease after swelling has been present for three or four weeks that it can be certain osteomyelitis will not develop. In these cases difficulty may also arise from the radiographic appearance of a small flake of alveolar bone at the site of an extraction. This flake of bone is frequently mistaken for a sequestrum but in fact it is traumatic in origin; a sequestrum is never evident radiographically in three weeks and such an appearance in the early stages of swelling of the jaw is not evidence of osteomyelitis.

(2) *Chronic localised osteomyelitis* of the mandible differs markedly from the diffuse or spreading type of the disease. The onset of chronic osteomyelitis is insidious, the symptoms are not so severe and a period of many months may elapse before the patient seeks advice. Dental extraction precedes the onset of symptoms in only 50 per cent. of these cases. In other cases the patient may have been edentulous for as long as 35 years, yet even in these circumstances the infection may commence around a buried root.

Chronic osteomyelitis also affects the two sexes equally, but occurs in patients of an older average age than those affected by the subacute type. In my own cases no patient was below 40 and the majority were over 50 years of age. *Pain* and *swelling* of the jaw are again the main symptoms. The *pain*, however, is not usually severe, does not radiate to the ear and numbness in the mental region is seldom noticed. The *swelling* is more localised and usually of the bony type with local tenderness. Some soft tissue induration may be present and an external sinus develop, thus causing difficulty in differentiating the disease from actinomycosis. Radiographs, however, will serve to distinguish these two conditions. The bone appears normal in actinomycosis, while in chronic osteomyelitis there is always radiographic evidence of bony destruction by the time the patient presents himself for treatment.

The *radiographic changes* in chronic osteomyelitis of the mandible are extremely varied. The disease may affect the alveolar margin alone, usually with sequestrum formation. Less commonly the inferior margin of the jaw is involved. In other cases there is a localised area of bone destruction in the mandible, in relation to a buried root and surrounded by an area of sclerosis, an appearance similar to that of Brodie's abscess. If the area of disease affects a narrow segment of the body of the mandible pathological fracture may be present. Occasionally, a more diffuse area of the jaw is involved and shows intermingling zones of rarefaction and sclerosis, with or without sequestration.

## TREATMENT

(*a*) *Diffuse or spreading osteomyelitis.* Before Mowlem (1944) advocated radical surgery for this type of disease the age-long teaching had been almost exclusively in favour of expectant conservative treatment. Most patients were thus exposed to unnecessary and prolonged suffering, morbidity or total disability extending over many months or years, multiple minor surgical interventions to drain abscesses or remove sequestra, and often an end-result of permanent disfigurement. This conservative treatment is dead and should never be resurrected.

There is great danger, however, that it will be resurrected under cover of that modern panacea, penicillin. Greer Walker (1947) prophesied that "the use of penicillin systemically without surgical interference will be the method of choice in the future." This is a statement of grave importance, for in my experience systemic penicillin, without surgical interference, does *not* stay the relentless progress of the disease. On many occasions I have seen patients with subacute osteomyelitis of the mandible given full doses of penicillin, and, although pain was sometimes relieved, bone destruction proceeded unchecked, the area of disease extended and even pathological fracture occurred in some cases. The radiographs in Fig. 1 illustrate the dangers of delay in operative treatment whilst penicillin is being administered. This patient had subacute osteomyelitis following extraction of the left lower first molar tooth. Two weeks after the extraction a correct diagnosis was made because of persistent pain in the jaw, bony swelling and tenderness, and a discharge of pus from the socket. A full course of systemic penicillin was begun and the lower radiograph, taken at this time, shows minimal bone destruction. The upper radiograph, taken after eleven days of penicillin therapy, shows extensive disease from the second molar to the first premolar region, a pathological fracture has occurred, and a large portion of alveolar margin has separated as a sequestrum. In spite of early diagnosis, early exhibition of full doses of penicillin, relief of tension within the bone by free drainage of pus into the mouth, and an infection by a staphylococcus subsequently shown to be penicillin-sensitive, this gross extension of disease took place.

In my opinion Greer Walker has made the mistake of trying to compare subacute osteomyelitis of the mandible with acute osteomyelitis of a long

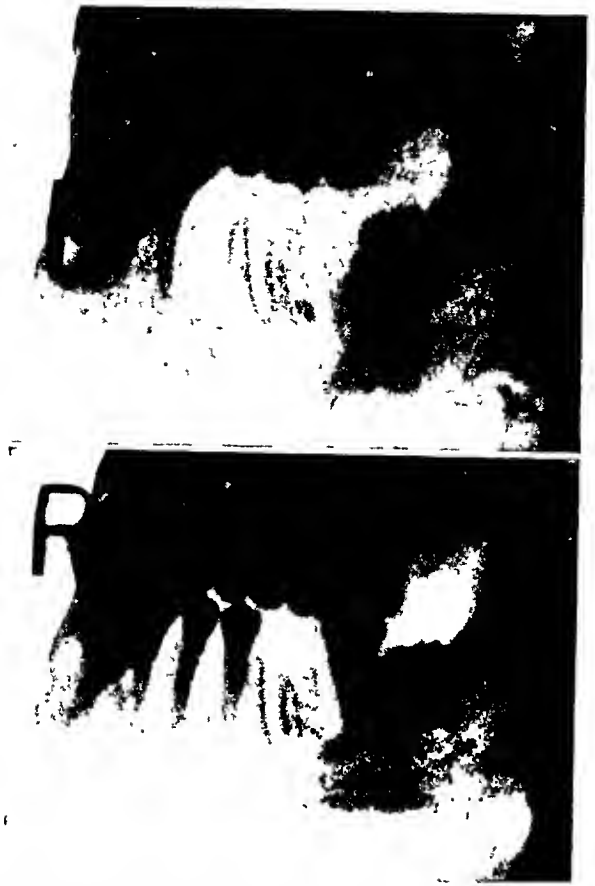



Fig. 1. Radiographs of osteomyelitis of the mandible. *Lower*: Two weeks after onset of infection, showing localised disease in the first molar region. *Upper*: Eleven days later, after full course of systemic penicillin, showing extension of disease with sequestration.

bone, and these two conditions are not strictly comparable. In acute osteomyelitis of a long bone penicillin undoubtedly rids the blood stream of infection and controls the systemic manifestations of the disease. In these respects it has proved a life-saving measure. In osteomyelitis of the mandible there is no blood stream infection or serious systemic disturbance and penicillin has no life-saving role to play. In osteomyelitis of a long bone penicillin will only, with certainty, produce resolution of the local disease if given within 24 or 48 hours of the onset; given later in the disease local infection may still progress and late operations of one type or another will often be necessary; whilst if the penicillin is not given until radiographic evidence of bone disease is present, surgery will almost always be required.

In osteomyelitis of the mandible the same remarks are true. If penicillin could be given within 24 or 48 hours of the onset of swelling of the jaw there is no doubt that osteomyelitis could often be aborted, but the diagnosis of osteomyelitis of the jaw cannot be made at this early stage.

When the diagnosis is considered in such cases and penicillin given with success, I believe that many simple alveolar abscesses are aborted whilst credit for curing osteomyelitis is claimed. It is, of course, ideal to recognize acute and subacute swellings of the mandible within 24 or 48 hours and to give penicillin in full doses; nevertheless, in many cases the penicillin will have been given unnecessarily and in others it may so mask the developing physical signs as to delay the diagnosis and proper surgical treatment of spreading osteomyelitis. When penicillin is given later than 48 hours after the onset of swelling of the jaw, and certainly when it is given after the appearance of radiographic evidence of bone disease, it will seldom cure osteomyelitis of the mandible without accessory surgical interference. In these later stages of osteomyelitis vascular thrombosis is likely to have occurred; and as the mandible is supplied by a single artery access of the drug, even to a sensitive organism, cannot be guaranteed. If bone necrosis is present, although the organism is reached and inhibited by penicillin, sequestra themselves will keep up a suppurative inflammation of bone and surgery will be required to eradicate the disease.

I believe, therefore, that the treatment of subacute osteomyelitis of the mandible should be by systemic penicillin combined with radical operation. The operation aims to remove all diseased bone and granulation tissue and to relieve tension, thus preventing further spread of the disease. I also believe that operation should be performed at the earliest opportunity, as soon as a definite diagnosis can be made. If the disease is suspected but a definite diagnosis cannot be made, penicillin should be given. The patient should then be kept under close clinical and radiological observation and operation undertaken as soon as the presence of bone necrosis is established. Only by these methods can the extent of the disease be kept within minimal limits and pathological fracture prevented with certainty. By waiting until gross bone destruction is present the operation itself may cause fracture of a jaw already weakened by extensive disease. Although the majority of pathological fractures unite quickly after the eradication of infection, a minority fail to unite altogether; and in any case a pathological fracture considerably prolongs the period of treatment.

(*b*) *Chronic osteomyelitis.* In cases of chronic localised osteomyelitis of the mandible the subject of treatment is less controversial. On account of the sclerosis of bone present in these cases it is generally agreed that penicillin will not gain access to the infected area and that surgical interference is required. If the disease is confined to the alveolar margin an intra-oral approach is used, but in most other cases, and in the vast majority of cases of diffuse or spreading osteomyelitis, I am in favour of an external approach on account of the better access it affords.

## RESULTS

To substantiate my claims for the merits of operative treatment the following brief review of results is submitted. I have treated 51 cases of

dental osteomyelitis, 33 of the subacute spreading variety and 18 chronic localised infections. All the patients have been subjected to operative interference and all have shown definite radiological evidence of bone disease. A few patients were seen when swelling of the jaw had been present only for two or three weeks, but the majority had had symptoms for six weeks or more. In the chronic cases the disease had been in progress for several months. Many of the patients in both groups had received penicillin treatment before coming under my care and it had failed to prevent extension of the pathological process.

Among the 33 patients with subacute osteomyelitis, 15 showed swelling of the bony type with minimal involvement of the soft tissues. These 15 patients all had good results, and the external wound healed by first intention in every case. Twelve of the 15 were free from symptoms and fit for work two weeks after operation. One patient had a pathological fracture before operation and this healed in four weeks. The other two patients had to undergo second operations because insufficient bone had been removed in the first instance, and they were away from work 8 weeks and 10 weeks respectively. The remaining 18 patients with subacute osteomyelitis showed gross swelling of the soft tissues around the jaw, and in these cases the disability period was more prolonged. In two of the patients, treated before penicillin was available, the wound was packed open and allowed to heal by granulation; in both cases second operations were necessary to remove more diseased bone and the disability period in each case was three months. In three patients soft tissue abscesses were incised before the bone operation was performed; the wounds after the bone operation healed by first intention but swelling was slow to subside and the disability period was 8 to 10 weeks. In three further patients pathological fracture was a complicating feature, present before operation in one case and produced at operation in two; two of these patients obtained rapid union and were fit for work in eight weeks, but the third fracture remained un-united and two subsequent bone-grafts failed. Eight patients in this group showed primary union of their wounds and all swelling had subsided in 4-6 weeks. Two patients required three operations each for recurrent infection of the bone or soft tissues, one as long as three years after the original operation; these patients therefore suffered recurring periods of disability but both had advanced disease before presenting for initial treatment.

Among the 18 patients with chronic localised osteomyelitis, 14 showed rapid healing and were back at work in 2-4 weeks. One patient required a second operation for residual soft tissue abscess and complete recovery was delayed for six weeks. The remaining three patients had each developed a pathological fracture before operation; one of these fractures united after splinting for two months, the other two remained un-united after three months' immobilisation. Fortunately, these un-united fractures were in the anterior region of the jaw and deformity was minimal; both patients had so little trouble that they refused a grafting operation.

## SUMMARY OF RESULTS

(*a*) *Subacute (diffuse or spreading) osteomyelitis—33 cases.*

(1) *15 cases* with bony swelling only (minimal involvement of soft tissues):

12—primary union of wounds: all signs and symptoms disappeared in 2 weeks.
1—pathological fracture before operation: disability 4 weeks.
2—second operations required: disability 8 and 10 weeks.

(2) *18 cases* with gross involvement of soft tissues:—

8—primary union of wounds: all signs and symptoms disappeared in 4-6 weeks.
2—pathological fractures (1 before, 1 at operation): disability 8 weeks.
3—preliminary incision of soft tissue abscesses: healed in 8-10 weeks.
2—before penicillin available: wounds packed open: disability 12 weeks.
1—pathological fracture occurred at operation: remains un-united: continuing disability.
2—three operations each for recurring infection: recurrent periods of disability.

(*b*) *Chronic localised osteomyelitis—18 cases.*

14—primary union of wounds: all signs and symptoms disappeared in 2-4 weeks.
1—second operation for residual soft tissue abscess: disability 6 weeks.
1—pathological fracture before operation: healed in 8 weeks.
2—pathological fractures before operation: remain un-united but no disability beyond 12 weeks.

These results are not perfect and it is hoped that greater experience will lead to improvement in the future. It is my thesis, however, that in subacute osteomyelitis of the mandible, the results of surgery combined with penicillin are better than those of penicillin alone; that in the cases reviewed surgery has succeeded where penicillin has failed; and that penicillin alone will continue to fail unless the limitations of its usefulness are recognised.

---

## REFERENCES

MOWLEM, R. (1944) *Brit. Med. J.* 1, 517.
WALKER, D. G. (1947) *Proc. Roy. Soc. Med.* 40, 309.

# A NOTE ON CYSTS OF ZEIS'S GLAND AND SEBACEOUS CYSTS IN GENERAL

by

Eugene Wolff, F.R.C.S.

ZEIS'S GLANDS ARE ordinary sebaceous glands attached to the follicles of the eyelashes and so the small rounded white tumours occurring at the anterior lid margin are usually described as cysts of Zeis's gland, just as quite commonly sebaceous cysts are still described without comment as being the result of distension of a sebaceous gland. Yet so long ago as 1897, S. G. Shattock wrote of wens or so-called sebaceous cysts of the scalp: "Part of the confusion that has arisen over the subject may be traced to the erroneous views sometimes held in regard to the seat of sebaceous cysts . . . . The truth is that the common 'wen' is a cyst, arising in most cases in the hair follicle and not in the sebaceous gland, its keratinous contents being furnished by the follicle which is lined with an extension of the general epidermis."

In the early stages the epithelium lining the cyst is exactly like that of the hair follicle. (Probably as in Fig. 1.)

Fig. 1. Portion of the wall of the same cyst as Fig. 2. In the epidermis there is what is probably an early stage of another cyst.

As the cyst grows the epithelium becomes generally flatter but the eleidin layer can still be made out (Fig. 2).

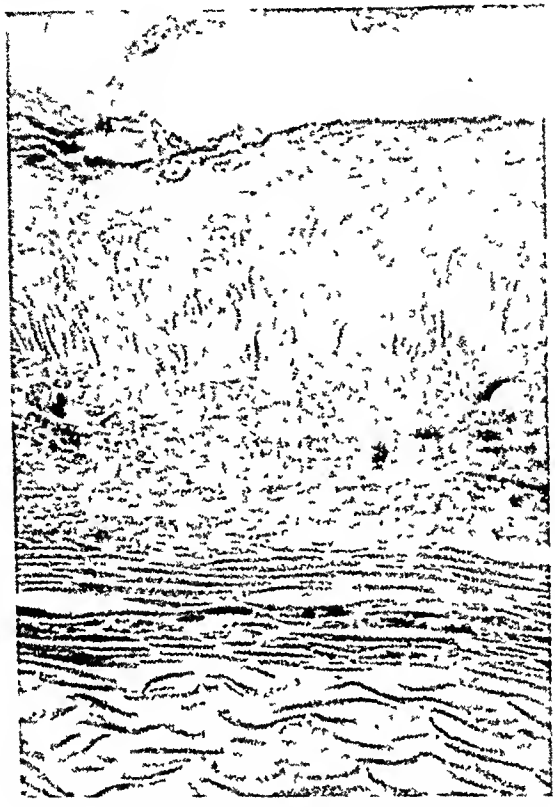


Fig. 2 Portion of wall of a cyst of Zeis's gland. The eleidin layer in its lining epithelium is still well marked.

With further distension the cyst eventually becomes lined with only one or two layers of nondescript cells.

The sebaceous gland attached to the follicle appears as a rule to atrophy and remains of it are occasionally found in the wall of the cyst. The cyst of Zeis's gland then is also formed by the keratinising contents of the distended follicle belonging to a cilium—either a lanugo or ordinary hair. That this is so is further shown by the white colour of the cyst, which is that of heaped up keratin. In this connection it is thus interesting to note that there is no histological difference between a milium and a sebaceous cyst.

SHATTOCK, S. G. (1897) Keratinising Epithelial Tumour of the Scalp. *Trans Path. Soc.* 33, 290.

## " OBSERVABLES " AT THE ROYAL COLLEGE OF SURGEONS

### (13) A BRONZE ÉCORCHÉ STATUETTE

ANATOMICAL FIGURES without skin for the study of the muscles were modelled quite frequently in Italy in the sixteenth century. They were described as écorché (O.F. escorchier, to strip off bark, to flay, to skin; LL. excorticare; L.Ex. from; cortex-icis, bark:—because the skin falls off when scorched).

Écorché statuette in the possession of the College.

There is a well-known écorché model of a kneeling figure by Michael Angelo. It was introduced by Alfred Gilbert, R.A., into his design for the bust of John Hunter which he was commissioned by St. George's Hospital to execute in 1893 at the time of the celebration of the centenary of John Hunter's death. The bust stood for some time in the Board Room on a pedestal designed by Gilbert but was afterwards moved to the outer gateway of the Medical School where it now stands—plain for all folk to see.

The bust of John Hunter over the gateway of St George's Hospital Medical School

Gilbert may have known that there was an écorché figure in the original Hunterian Collection—a late sixteenth-century Italian bronze representing a standing figure 9¼ inches in height. According to Sir Eric Maclagan, late Director of the Victoria and Albert Museum, it is probably by Marco d'Agrate, a pupil of Michael Angelo. The figure used to be kept in the Museum of the College. It was listed in the catalogue of 1850 but not in that of 1862, so must have disappeared between those dates. It was bought back by the College in 1912 from Mr. C. S. Stanford Webster, F.I.C. who found it among the effects of his father, Mr. Thomas Webster, M.R.C.S., L.R.C.P. to whom it had been given by Miss Baily in part payment of fees. Miss Baily had acquired the statuette on the death of her father, Mr. E. H. Baily, R.A. a sculptor, to whom, Mr. Webster stated, it was lent by Sir Richard Owen. Thus, over half a century after its disappearance it returned to its spiritual home. It then found a safer resting place in the Conservator's Room, from which it would be missed at once if it disappeared again. It now adorns the mantel-shelf in the President's Room, and again its removal would immediately be noticed.

John Hunter may have acquired the figure from his brother, for it is depicted by Mason Chamberlin, R.A. in his portrait of William Hunter in the Council Chamber of the Royal Academy (here reproduced). An engraving of this picture by Joseph Collyer, A.R.A. has recently been purchased by the College.

W-J.

*By kind permission of The Royal Academy.*

## MONTHLY DINNERS

Monthly dinners are held in the College on the second Wednesday of each month. The following are entitled to attend with their guests: *All Diplomates* and students of the College, and Members of the Associations linked to the College through the Joint Secretariat. It is not necessarily intended that guests should be members of the medical profession.

The dinners will be at 7 p.m. on the following Wednesdays: February 9, March 9, April 6, May 11, June 8, and July 13, 1949. There is an inclusive charge of £1 5s. (including drinks), which must be sent with the application to the Assistant Secretary at least a week before the date of the dinner. The dress is Lounge Suit or Uniform.

---

## *DIARY FOR JANUARY* (19th-31st)

| | | | |
|---|---|---|---|
| Wed. | 19 | 5.00 | MR. L. W. PROGER—Erasmus Wilson Demonstration—New additions to the Museum.* |
| Fri. | 21 | | Final L.D.S. Examination (Part I) begins. |
| Mon. | 24 | 5.00 | DR. A. SCHWEITZER—Cardiac Mechanics. |
| | | 6.15 | PROF. J. WHILLIS—Functional Activities involving the Mouth and Pharynx. |
| Wed. | 26 | | Primary F.R.C.S. Examination begins. |
| | | 5.00 | PROF. D. T. HARRIS—Respiration (Part 1). |
| | | 6.15 | DR. D. LONG—The Application of Penicillin to Dentistry. |
| Thur. | 27 | 5.00 | MR. R. J. LAST—Anatomy of the Larynx. |
| | | 6.15 | PROF. D. T. HARRIS—Respiration (Part 2). |
| Fri. | 28 | | Final L.D.S. Examination (Part II) begins. |
| Mon. | 31 | 5.00 | PROF. G. PAYLING WRIGHT—Spread of Infection in Tissues (Part 1). |
| | | 6.15 | DR. C. H. TONGE—Anatomy of the Oral Cavity. |

---

## DIARY FOR FEBRUARY

| | | | |
|---|---|---|---|
| Tues. | 1 | 5.00 | PROF. G. PAYLING WRIGHT—Spread of Infection in Tissues (Part 2). |
| | | 6.15 | DR. C. H. TONGE—Anatomical Considerations in relation to the Technique of Regional Anæsthesia as applied to Dental Surgery. |
| Wed. | 2 | 5.00 | PROF. T. CAWTHORNE—Hunterian Lecture—Some Observations on the Pathology and Surgical Treatment of Labyrinthine Vertigo of Non-Infective Origin.* |
| Thur. | 3 | 5.00 | DR. C. C. N. VASS—Saliva and Salivary Secretion. |
| | | 6.15 | PROF. R. HARE—Streptococcal Infection. |
| Fri. | 4 | | D.O.M.S. Examination (Part I) begins. |
| Mon. | 7 | 5.00 | PROF. R. W. RAVEN—Hunterian Lecture—The Properties and Surgical Problems of Malignant Melanoma.* |
| | | 5.00 | DR. R. L. WATERFIELD—Reaction of Blood Cells to Trauma and Infection. |
| | | 6.15 | MR. E. B. MANLEY—Development and Growth of the Teeth (Part 1). |

* Not part of courses.

| | | | |
|---|---|---|---|
| Tues. | 8 | 5.00 | MR. E. B. MANLEY—Development and Growth of the Teeth (Part 2). |
| | | 6.15 | PROF. J. Z. YOUNG—Structure and Function of Peripheral Nerves. |
| Wed. | 9 | 5.00 | PROF. HENRY COHEN—Moynihan Lecture—Hypoglycæmia and Hyperinsulinism.* |
| | | 7.00 | Monthly Dinner for Fellows, Members and Licentiates (see page 63). |
| Thur. | 10 | 5.00 | PROF. MICHAEL OLDFIELD—Hunterian Lecture—Advances in Hare-lip and Cleft Palate Surgery, following the Treatment of 500 Patients.* |
| | | 5.00 | DR. K. C. RICHARDSON—General Histology in relation to the Oral Cavity. |
| | | 6.15 | PROF. J. H. DIBLE—Inflammation and Repair. |
| Fri. | 11 | | D.O.M.S. Examination (Part II) begins. |
| Mon. | 14 | 5.00 | MR. H. S. SOUTTAR—Hunterian Oration—John Hunter The Observer.* |
| Tues. | 15 | 5.00 | DR. J. DOUGLAS ROBERTSON—Metabolism Disorders in Thyroid Disease. |
| | | 6.15 | PROF. JOHN KIRK—Fascial Planes of the Neck. |
| Wed. | 16 | 5.00 | PROF. G. PAYLING WRIGHT—Repair of Connective Tissues. |
| | | 6.15 | DR. R. L. WATERFIELD—Blood—Physiological Aspect. |
| Thur. | 17 | 5.00 | PROF. J. G. BONNIN—Hunterian Lecture—Diastasis of the Tibio-Fibular Syndesmosis.* |
| Fri. | 18 | 5.00 | DR. J. DOUGLAS ROBERTSON—Calcium Metabolism. |
| | | 6.15 | MR. A. BULLEID—The Application of Bacteriology to Dental Procedure. |
| Mon. | 21 | 5.00 | PROF. D. F. ELLISON NASH—Hunterian Lecture—The Development of Micturition Control.* |
| | | 5.00 | PROF. H. H. STONES—The Diagnosis and Treatment of Pathological Conditions of the Pulp (Part 1). |
| | | 6.15 | DR. GEOFFREY ORGANE—Anæsthesia in relation to Dental Surgery. |
| Tues. | 22 | 5.00 | PROF. H. H. STONES—The Diagnosis and Treatment of Pathological Conditions of the Pulp (Part 2). |
| | | 6.15 | MR. V. ZACHARY COPE—Actinomycosis. |
| Wed. | 23 | 5.00 | PROF. W. S. LEWIN—Hunterian Lecture—Acute Subdural and Extradural Hæmatoma in Closed Head Injuries. |
| Thur. | 24 | 5.00 | PROF. R. ROAF—Hunterian Lecture—The Treatment of Residual Disability following Injuries of the Peripheral Nerves of the Upper Extremity.* |
| | | 5.00 | MR. H. T. ROPER-HALL—Therapeutics in Dental Surgery. |
| | | 6.15 | MR. R. J. MCNEILL LOVE—Cervical Glands in relation to Dental Surgery. |
| Mon. | 28 | 5.00 | PROF. R. A. RUSSELL TAYLOR—Hunterian Lecture—The Ætiology, Pathology, Diagnosis and Treatment of Acute Pancreatitis: a Review of 110 Cases.* |
| | | 5.00 | MR. MYLES L. FORMBY—Sinusitis and Allied Problems in relation to Dental Surgery. |
| | | 6.15 | DR. A. C. ROXBURGH—Skin Diseases in relation to Dental Surgery. |

* Not part of courses.

# PROCTOLOGY THROUGHOUT THE AGES

Bradshaw Lecture delivered at the Royal College of Surgeons of England

on

11th November, 1948

by

L. E. C. Norbury, O.B.E., F.R.C.S.

Vice-President, Royal College of Surgeons of England

Consulting Surgeon, Royal Free Hospital and St. Mark's Hospital

THE BRADSHAW LECTURE was founded by the late Mrs. Sally Hall Bradshaw, widow of Dr. William Wood Bradshaw, in memory of her husband, who for many years practised in Reading. He qualified as a Member of this College in 1833, and was elected to the Fellowship without examination in 1854.

The subject I have chosen for my lecture is:

"PROCTOLOGY THROUGHOUT THE AGES"

I have long been interested in the science of proctology, and it has given me great pleasure, and at the same time has been a valuable education, to delve into the history of the past, and to realise with astonishment the profound knowledge possessed by those who practised the "art of medicine" in the centuries before Christ. It is, of course, impossible to give more than a résumé of the growth of proctology within the allotted span of a lecture, and therefore I propose only to pick out salient facts which appear to me of foremost interest and importance in tracing the science of proctology from its inception to the present day.

J. F. Montague, in his paper on "The Origin of Rectal Specialists, and the Future of Proctology,"(1) states that:

> The earliest mention of the study of "Rectal Diseases" is to be found in the "Code of Hammurabi," written about 2200 B.C. In this there are instructions to the patient to the effect that he should "pay the doctor five shekels for curing him of a diseased bowel."

*Hæmorrhoids* are mentioned more particularly in the famous "Ebers Papyrus," which was written in Egypt about 1500 B.C. It is said that the Hindus had a clinical knowledge of hæmorrhoids and fistula as early as 1000 B.C.

It is interesting to note that the Bible was probably the first textbook on rectal diseases, for in the Second Book of Chronicles there is a short clinical description of "Rectal Prolapse," as follows:

> "And thou shalt have great sickness by disease of thy bowels, until thy bowels fall out by reason of the sickness day by day."

Again, in Deuteronomy and Samuel, occur words which were rendered into English as "Emerods" by the old translators of the King James version, and generally regarded as meaning "hæmorrhoids" or piles.

Since the dim dark ages, two topics beyond all others have engaged the attention of rectal surgeons, namely, *Fistula* and *Piles*.

Hippocrates was born in the island of Cos about 460 B.C. He claimed descent from the god Æsculapius on his father's side, and from Hercules on his mother's side. He is said to have died at Lorisson in Thessaly at the age of 104.

More than 60 existing writings are attributable to him.(2) Most, it is said, were composed by his disciples. Hippocrates stressed the importance of practising with either hand, so as to be ambidextrous —a most useful accomplishment in rectal operations.

Some of the aphorisms of Hippocrates dealing with rectal conditions are most interesting. "An aphorism" was defined by the three ancient commentators, Theophilus, Meletius and Stephanus, as "a succinct saying comprehending a complete statement," or in other words, "a saying, poor in expression, but rich in sentiment." Galen pronounced an aphorism to be "a writing of great power comprehended in a few words." In modern language it is a "writing remarkable for brevity and point." As bearing on my subject, I would mention the following aphorisms:

> "The Hæmorrhoids happening to melancholick and nephritick persons are good. By the hæmorrhoids the super-abundant blood is evacuated. If they are suppressed, they cause melancholy—pains in the back and loins—stone and gravel."

Another aphorism of Hippocrates is as follows:

> "Hæmorrhoids that have long continued to flow must not be healed up quite, but one vessel may be kept open, or else there is danger that a dropsy or consumption will succeed."

One can argue from this that Hippocrates had some knowledge of the association of certain conditions of the liver with piles. Hippocrates attributes "Fistula-in-Ano" to "Tubercles" or to injuries inflicted on the parts adjoining the anus in riding, rowing or from any such act of violence. The so-called "Tubercle of Hippocrates" was undoubtedly an ischio-rectal abscess. Hippocrates' account of the treatment of ischio-rectal abscess and fistula holds good to-day. He stresses the importance of early incision of an ischio-rectal abscess and the importance of preventing too early healing of a fistula.

On the treatment of "Fistula," the method advised is as follows:

> "Twist round a fivefold strand of raw linen some horse-hair, that it may not decay. Insert this by means of a pewter probe through the fistula. Tie the ends close to the anus—tighten every day until the fistula is entirely destroyed. A sponge covered with honey is introduced to prevent a coalition of the parts before they are entirely sound. In this way the fistula being forcibly expanded by the sponge will not fill up and heal unequally, but it will all become whole together."

The operation by the ligature was called "Apolinose." The ligature gradually divided the fistula, and at the same time by its irritative action it raised up a healthy reaction in the part; hæmorrhage from division of vessels was also avoided. This method of "Apolinose" is almost identical with our modern method employed in the treatment of certain cases of high-level fistula, especially the sub-mucous variety, when hæmorrhage at a depth would be difficult to control. Hippocrates advised the use of the knife if the method by ligature was ineffective.

Aulus Cornelius Celsus flourished in the golden age, that is to say in the reigns of the Emperors Augustus and Tiberius. He has been called the "Latin Hippocrates." He possessed a diversity of talent. He composed works on the military art, on rhetoric, and on agriculture, as well as medicine. Celsus also advocated the gradual division of a fistula-in-ano by a thread passed through the track and gradually tightened. He recommends that the patient "walk about and attend to his business as if in perfect health," thus anticipating our modern method of getting the patient up early. The difficulties and dangers of operating upon a fistula with a high internal opening were appreciated 19 centuries ago. The dictum of Celsus holds good in essence at the present day.

Paulus Ægineta(3) lived 1,000 years after Hippocrates. He wrote a "Treatise of Surgery" about A.D. 600. He recommends passing a sound along the fistulous track and making it complete by pushing the point through the anal canal and cutting down on the track. He also advised "excision of the callus track" (another advance in the treatment of fistula). Ægineta was of opinion that all fistulæ, except the most complicated, in general, were easily cured. In contrast to this optimistic statement of Ægineta, William de Salicet (1245), wrote: "When the fistula is complete it is assuredly so difficult to cure, that it is better and more honourable for the surgeon to give up the case at once." This, in part, holds good to-day in the case of certain complicated fistulæ. One, Avicenna, favoured the ligature method for fistula. He preferred to use the "bristles of a hog," instead of a linen thread, since he said they would not putrefy.

The pathology of hæmorrhoids is described in the works of Hippocrates. The operation for their removal by the "cautery" is considered in some detail.

It is recommended to place the patient on his back, force out the anus as much as possible with the fingers, make the irons red-hot (the ancient cautery was disc-shaped), and burn the pile until it be dried up.

When applying the cautery, "the patient's head and hands should be held so that he may not stir, but he himself should cry out, for this will make the rectum project the more."

The word "shawl" is used extensively in the works of Hippocrates, as a means of keeping on the dressing and for support. This presumably corresponds to our present-day "triangular bandage."

It is to be noted that Celsus recognised a condition of " anal cracks " associated with pruritus ani. He describes the condition as " a most tedious malady." (All proctologists will agree with this.) One method of treatment advised is the application of hot hard-boiled pigeon's eggs with their shells removed.

" The Papyrus Ebers " is regarded as the greatest Egyptian Medical Document. The time of writing was about 1550 B.C. References are made in it, however, to writings of a much earlier date, such as 3000 B.C. In this papyrus, reference is made to the use of " Suppositories to be put in the hinder part " as a remedy to expel " Burning in the anus."

The suppository contained juniper, frankinsense, yellow-ochre, cuttle-bone, cumin, honey, myrrh and cinnamon.

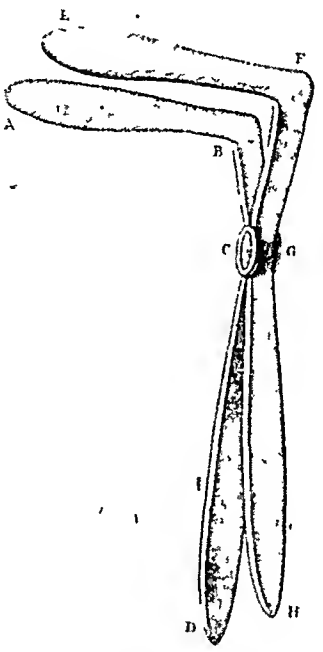



Fig 1. Bronze speculum.

Suppositories were also recommended and employed for the treatment of hæmorrhoids, and " to heal the anus when it is ill."

Amongst the ruins of Pompeii numerous surgical instruments were discovered, including a " speculum ani " in bronze.(4) This speculum, along with other instruments, was described by Vulpes in a series of communications to the Royal Academy of Archæology at Herculaneum in 1846-7.

It will be recalled that Pompeii was overthrown by an earthquake in A.D. 63, was rebuilt, but buried again by an eruption of a volcano in A.D. 79, and rediscovered in 1748.

History does not reveal any great advance in the art and science of proctology until the time of John Arderne.

Arderne was born in 1307. He wrote several works, which were collected and edited by the late Sir D'Arcy Power.

Arderne lived to nearly the end of the 14th century. He practised in Newark from 1349 to 1370. Before settling in Newark he was a surgeon in the service of Henry Plantagenet. He was a sound, practical surgeon, who carried out his work by methods not very different from those of the modern aseptic surgeon. He taught that "wounds should heal without suppuration"—that local applications to them should be as little irritating as possible, and that the dressings should be infrequent.

He was the first surgeon to abandon the use of corrosive agents in the cure of fistula. Much of his success was probably due to this. He had

Fig 2. Picture of 14th century surgeon operating for fistula.

sufficient originality to invent the operation for the cure of fistula, which, after falling into disuse for nearly 500 years, is now universally adopted.

Arderne(5) employed both the ligature and the knife in the treatment of fistula. He was quite prepared to tackle complicated fistulæ, for he cured one, Thomas Braine, that had 15 holes, eight on one side and seven on the other, by which "wynde went out with egestious odour." Arderne gives some practical advice to the contemporary rectal surgeons as regards fees. He says: "For the cure of a fistula-in-ano, when it is curable, ask he competently of a worthy man and grete, one hundred

mark—of less men, forty mark, and take not less than one hundred shilling, for never in my life took I less than an hundred shilling for cure of that sickness."

Arderne's writings constitute a landmark in rectal surgery. He is the first to give a list of cases he had cured. The description of his methods is clear.

In Hume's "History of England," it is stated that Henry V, who died in 1422, at the age of 35, died from the effects of a fistula "which surgeons at that time had not the skill to cure." In so short a time had Arderne's principles and practice been forgotten.

After Arderne, there is little to note till the early 18th century, when Heister of Helmstadt published an excellent work on surgery, which was translated into English in 1743. Heister gives a good account of the varieties of fistula. He advises injecting "milk, if it be so crooked that a probe cannot follow it," thus anticipating our more modern method of injection with methylene blue, or lipiodol. He is in favour of using a falciform knife with an obtuse point, such as was used by Félix on Louis XIV for the cure of fistula in 1686, and was afterwards called the "Bistouri Royal."

*Fig. 3. Bistouri Royal.*

(Illustration: Selected Papers of St. Mark's Hospital)

Heister quotes from Dionis(6), who says that "The French were so fond and proud of being in the fashion when their King Louis XIV had a fistula, that they boasted of the disorder as a "Point of Honour," and would even undergo the operation when there was no real necessity. Heister comments on the difficulty of healing a fistula with a high internal opening. He says that the operation of cutting cannot well be performed without hazarding the life of the patient. He states that it is wise to refrain from using the knife in such cases, which might cause a fatal hæmorrhage. He also emphasises the importance of "the external incision being larger than the internal, that there may be free access to cleanse and dress to the bottom of the sinus. It also may be necessary to extirpate the callous parts." These are principles which, in the main, hold good to-day. It is the practice amongst many rectal surgeons

to pass a ligature along a deep sub-mucous track by means of a threaded probe, and to tie this tightly in order to gradually cut through the track and so avoid deep-seated hæmorrhage which might result from division with the knife and which would be difficult to control.

John Hunter (1728-1793) had certain views as to the causation and treatment of "Piles," as instanced by the following extract from his case book (7): "George Watt, comb-maker, St. Martin's Court, aged 48, for some time troubled with the Piles and a Procidentia Ani: For 12 years past he has periodic bleeding from these parts, *which is always at the full-moon.* He knows when this bleeding is coming on for he is then out of order with respect to his health—his belly swells, he is oppressed, but by the loss of about a pint of blood he is in every respect easier. He is sometimes without his bleeding for half a year or more."

Another extract from the case book is as follows: "A young lad, eight years of age, much troubled with the Piles, which bled very much. About two years ago they entirely went away, but soon after the *veins of the tongue* became varicose and often bled. He came to 'St. George's Hospital,' and was ordered Nitre, and to wash his mouth with a solution of White Vitriol. A seton was passed, but he seemed to get better but slowly, so much so as hardly to expect success from this practice. He took some Tincture of Sara to bring on the Piles again, but it did not succeed. He was turned out for a misdemeanour. Hunter states that in all probability, if the hæmorrhoids could have been brought on again, the veins of the tongue might have been relieved."

Martin Van Butchell, a pupil of John Hunter, was born in 1735. He was apparently a man of many and varied activities. He successfully practised as a dentist for many years; he became eminent as a maker of trusses, and acquired celebrity by his skill in treating cases of "fistula." He was still more noted for his eccentricity of manners. He resided for many years in Mount Street, Berkeley Square, and attracted numerous patients by his quaintly worded advertisements in the newspapers. On the death of his first wife, her body was injected with coloured preservatives, and the mummy was kept in his parlour for many years and exhibited to his friends. On his second marriage, it was found expedient to remove the body to the Museum of the Royal College of Surgeons.

The following advertisement appeared in the *Morning Herald* of Wednesday, May 27, 1789:

Fistula-in-Ano
*No cure—No Pay*

This teazing local disease commonly called Fistula-in-Ano is radically cured, sometimes in a week, always in two.

*Van Butchell.*

FISTULA in ANO.
No CURE no PAY.

THE teazing, local Difeafe commonly called, a FISTULA in ANO, is radically cured, (fometimes in one week, always in two,) without cutting, dreffing, medicine, cautery, injection, rifk, confinement, lofs of blood, or an atom found parts;

Fo ... are, Sur-

... l-ftreet,
Phyfician Extraordinary to the Queen,
And Anatomical Lecturer to the Royal Academy.)
At his houfe, No. 56, Mount-ftreet, Grofvenor-fquare;
From Ten o'Clock till Two.

not too far from his) even, under the infpection of eminent Phyficians, Surgeons, and Licentiats in Midwifery, provided they, (as men of honor) will not defcribe, nor exercife his art.

Can refer to credible men, whom he has cured two years ago —One of them a neighbour, weighing twenty ftone. ... hours; nor at all,

F. R. S.
Wales;
Majefty;

Having, moft kindly (in confidence) attended to the particulars of a late cure, can favor his friends, with a decided opinion, of the method, and the man who caufes
Each bit of the complaint to go away
Leaving no trace behind—but gratitude.

To the Nobility, Gentry, and Public at large,
For the benefit of emaciated youth, and debilitated old age, whofe conftitutions have been broken, and reduced by too powerful courfes of mercury, exceffive drinking, or by thefe practices (too common amongft youth) which by relaxing the whole frame, bring on debility of body and mind, low fpirits, melancholy, lofs of memory, dimnefs of fight, pains in the back and loins, feblenefs, paralytic complaints, and the whole train of nervous diforder.
HUNTER's RESTORATIVE BALSAM

Fig. 4. Advertisement Van Butchell.

I am afraid we are not so optimistic about the cure of fistula at the present day. It is axiomatic amongst proctologists that " more reputations are lost in the treatment of fistula than with any other operation." How much surgery owes to the discoveries of Pasteur, Lister and Morton cannot be fully estimated. Without such discoveries, surgery would have made little, if any, progress.

The middle of the 19th century was the " Dawn of Anæsthesia." Nitrous oxide gas was first used as an anæsthetic by Wells, Rigg and Colton in 1844, although discovered by Priestly in 1772 ; ether by Morton in 1844, and chloroform by Simpson in 1847. In 1867 Lister published his article on " The Antiseptic Principle in the Practice of Surgery."(8)

William Allingham, in his text-book of 1888, states that in hospital practice fistula is the most common rectal disease affecting the adult. In recent years cases of fistula have considerably decreased in number, no doubt the result partly of an earlier recognition of ischio-rectal abscess and an appreciation of thorough and immediate incision as recommended by Hippocrates. Do our methods in the treatment of piles differ essentially from those of Hippocrates and Celsus ?(9) *Our radical treatment*, " the ligature," is described by Celsus, and *our palliative treatment*, " galls," was used by Hippocrates. We use the

"knife" for fistula as advised by Hippocrates, and Ernest Miles, in writings on fistula, recommends that a sub-mucous fistula with a high internal opening should be treated by "ligature."

In 1868, Demarquay strongly advised the red-hot cautery as a cure for internal piles. William Allingham, in the 5th edition of his book (1888) gives an exhaustive account of almost all the operations and methods of treating piles which have been tried.

He mentions 13—many are now obsolete.

The list includes: Injection Treatment; Clamp and Cautery; Whitehead's operation; Allingham, Junior's, modified Whitehead's operation, &c.

After having tried many methods, Allingham pronounces himself in favour of the ligature method.

Allingham gives the credit for its introduction into surgery to Salmon, in the year 1838. He states that at St. Mark's Hospital, there had only been one fatal case in 40 years of operating, i.e., one out of a total of 670.

Frederick Salmon was born at Bath in 1796. He received his medical education at St. Bartholomew's Hospital. ([10]) He became a member of the Royal College of Surgeons in 1818. He was especially interested in diseases of the rectum.

Fig. 5. Frederick Salmon.

Sir Charles Gordon-Watson, in an article on "Progress of Rectal Surgery"([11]) published in 1934, states that "London is the only city

in the world which possesses hospitals devoted exclusively to the treatment of Rectal Diseases." For this we owe a debt of gratitude to Frederick Salmon, founder of St. Mark's Hospital. In 1835 he founded an institution in Aldersgate Street with seven beds for the relief of the "poor afflicted with fistula and other diseases of the rectum." The Lord Mayor was its first president. It has ever since been the custom for the Lord Mayor in office to be president of the hospital. This was the beginning of St. Mark's Hospital, which was established in the City Road in 1854.

In this country we have no "pure proctologists." The two hospitals for rectal diseases, St. Mark's and the Gordon, are staffed by general surgeons.

There is much to be said in favour of regarding proctology as a speciality, but like all specialities it should not be divorced from the practise of general surgery.

St. Mark's Hospital since its inception can number various pioneers of the science and art of proctology on its staff. To mention a few: Peter Yeams Gowland; William Allingham (see Fig. 6); David Henry Goodsall; Frederick Swinford Edwards (see Fig. 7); Herbert William Allingham; Percy Furnivall; Percy Lockhart-Mummery (see Fig. 8); Charles Gordon-Watson (see Fig. 9).

### Injection Treatment for Piles

This did not originate, as is usually supposed, in America. It was first carried out by Mr. Morgan in Dublin in 1869. He employed iron persulphate.

In 1874 William Colles, a Dublin surgeon, injected a case of piles with iron perchloride.

*Carbolic Acid* was first used in 1871 by Mitchell of Illinois. The method was kept secret for some time, but was eventually sold to various unqualified people known as "*travelling pile doctors.*" In 1876 Professor Andrews of Chicago discovered the secret from one of the quacks, and carried out an exhaustive investigation. He collected the results of 3,300 cases.

Mitchell used one part of carbolic acid to two parts of olive oil. Most of the "irregulars" used strong solutions of carbolic acid, varying from 27 to 95 per cent. It took some 20 years before three definite schools of opinion on the subject were established.

*One school*, including William Allingham, considered the method unsafe and even dangerous.

*A second school* believed in injecting strong solutions of carbolic acid, i.e., over 20 per cent. and up to 95 per cent., the aim being removal of the piles by sloughing.

*A third school* advocated weak solutions of carbolic acid, i.e., from 5 to 20 per cent., injecting small quantities and aiming at producing mild irritative changes with ultimate fibrosis and shrinking of the piles.

Fig. 6. William Allingham

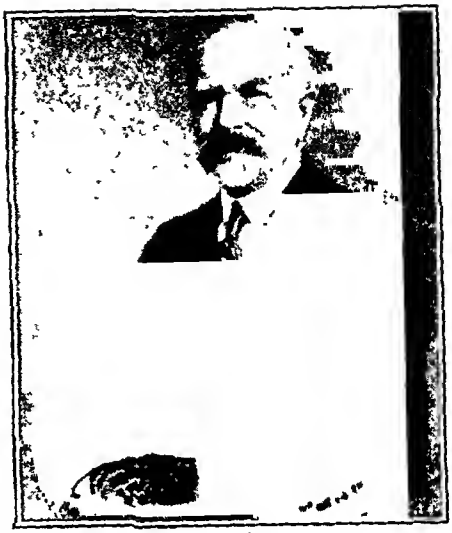


Fig. 7. Frederick Swinford Edwards.

Fig. 8. Percy Lockhart-Mummery.

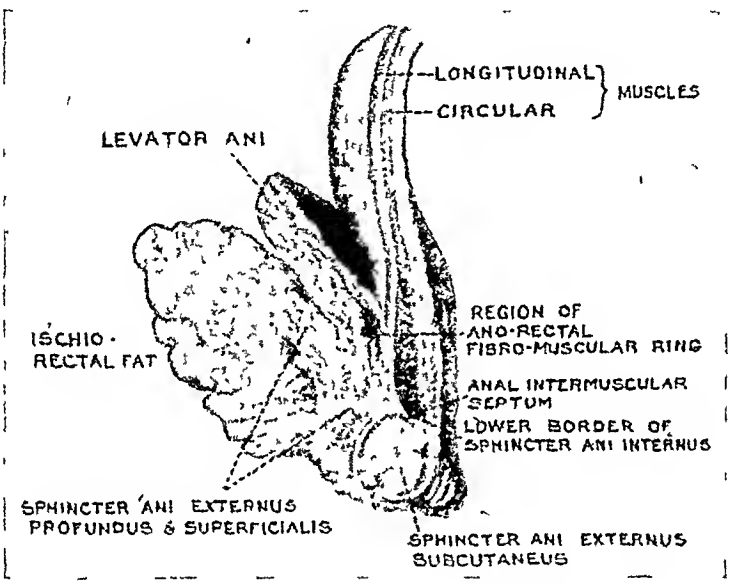
Fig. 9. Charles Gordon-Watson.

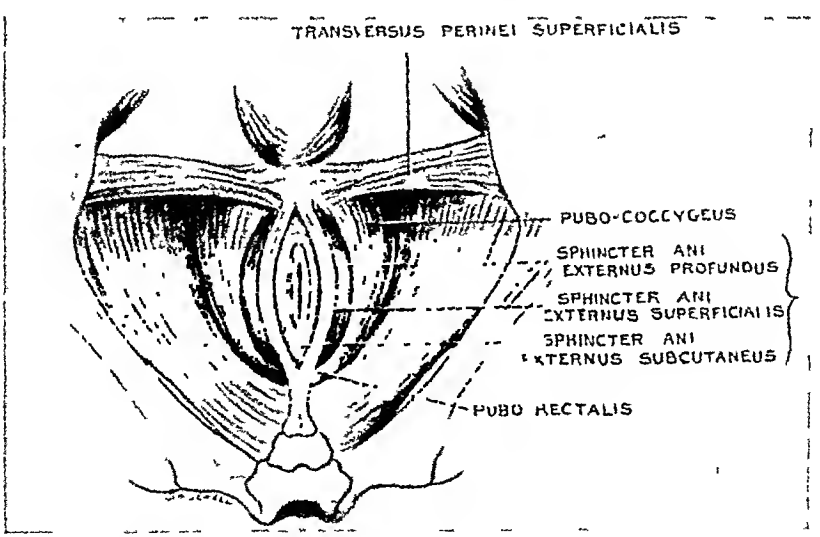
The "strong school" has been dying out, whilst the "weak school" has become more firmly established.

The researches of E. T. C. Milligan and C. Naunton Morgan into the surgical anatomy of the anal canal and rectum, have placed the operative treatment of ano-rectal fistula on a sound basis.(12) A thorough appreciation of the musculature of this region has enhanced the satisfactory and rational planning of operations for the cure of complicated fistulæ, so avoiding the danger of post operative incontinence. They stress the importance of recognising and preserving the "ano-rectal ring" in

order to retain control. Again, their researches have established on sound anatomical principles the modern "ligature operation for piles."

*The Sigmoidoscope.*—The introduction of the sigmoidoscope as a means of diagnosis, marks a landmark in the progress of proctology. Kelly, of Baltimore, was the first to utilise a sigmoidoscope of any practical value, although several patterns had been tried previously but were too complicated to be of any real service. Kelly's instrument was a long straight tube, 35 cms. in length, which had to be passed by "feel"—a




Figs. 10 and 11. Surgical anatomy of anal canal and rectum

dangerous procedure. Illumination was obtained by reflected light from a mirror on the forehead, and was most inefficient.

Marion Sims, in 1845, demonstrated to the world the advantages of atmospheric pressure in ballooning the vagina. The "Sims lateral-prone position," enabled this to be effective, as also the genu-pectoral position, which is so frequently adopted. Van Buren, in 1870, applied this method to the rectum. Allingham advised the use of this method for examination. To Kelly, however, belongs, not the invention of a tube, still less the discovery of the inflating power of atmospheric pressure, but their ingenious and practical application to rectal surgery.

*The Strauss pattern*, in which the light is carried on a wire to the distal end of the tube, is a form commonly used by proctologists. Its one disadvantage is contamination of the light by fæces. A more modern form is that of *Yeomans*, in which the illumination is proximal, thus avoiding any contamination of the light.

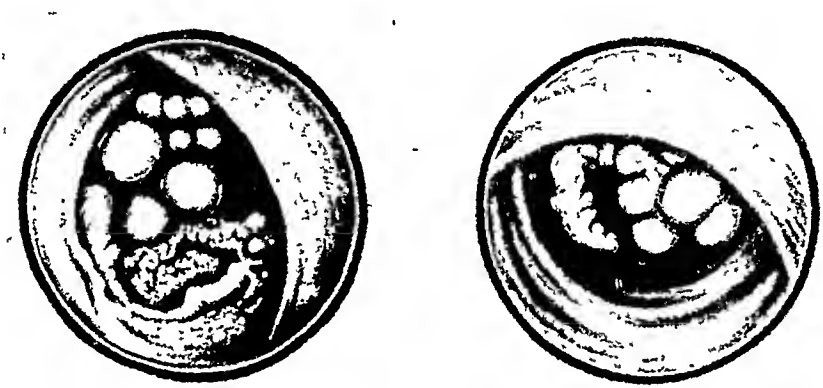


Fig. 12. Slide showing tumour through sigmoidoscope.

If for no other reason than the acquisition of skill in the use of the sigmoidoscope as a diagnostic agent, the proctologist serves a useful purpose. The early diagnosis of carcinoma by this means is of the highest importance, but equally the differential diagnosis and the pleasure and thrill of being able to tell the anxious patient that his rectal symptoms are not due to cancer, is to my mind of equal, if not greater, importance.

### Artificial Anus

Sabatier(13) in his "Memoires sur les anus contre-nature," in 1774, describes a case of "artificial anus," which developed in the right groin of a soldier, apparently following an operation for intestinal obstruction, performed by Mr. Bowland. Most of the excrement passed this way, and very little passed the true anus.

*Colotomy* was originally performed over 200 years ago, but has only been practised on a large scale since about 1860 as a means of obviating

death from intestinal obstruction. Its position as a recognised operation is mainly due to the efforts of English surgeons, notably Curling, Bryant and Allingham. The first suggestion of the operation was made by Littre in the year 1710. It does not appear, however, that he in effect performed colotomy.

Alexis Littre was born in 1658 and died in 1725. His name is often confused with that of Emile Littré (with an accent on the e), who wrote a Dictionnaire de Médicine and edited the "Works of Hippocrates" in 1839, translating them into French.

Fig. 13. Artificial anus (traumatic).

It was not till 60 years later that the operation was actually performed on the living subject by Pillore of Rouen, who opened the cæcum in the right inguinal region. The dread of opening the peritoneum, suggested to Callisen the possibility of utilising the descending colon, where it was uncovered by peritoneum in the left loin. He does not seem to have performed this operation on the living body. In 1797 Fine of Geneva opened the transverse colon by an incision in the umbilical region.

Subsequently Amussat published six cases in which he was able to open the colon without wounding the peritoneum, and five of these were successful. His first case was a right lumbar colotomy, using the ascending colon.

The operation of lumbar colotomy has since borne the name of this distinguished surgeon.

Littre's operation aimed at opening the cæcum or sigmoid colon by an incision in the right or left groin.

Various modifications in technical detail were suggested and practised by Cripps, Allingham, Jessett and others, in the performance of "inguinal colotomy." In all of these there was one decided disadvantage which did not attach to the older extra-peritoneal operation of Amussat, namely, delay in affording relief in cases of obstruction. Delayed opening of the colotomy for from one to six days, in order to obtain better healing of the wound, was suggested by Davies-Colley in a communication published in 1885.([14]) Paul noted the dangers and discomfort from delay in affording immediate relief in cases of obstruction.

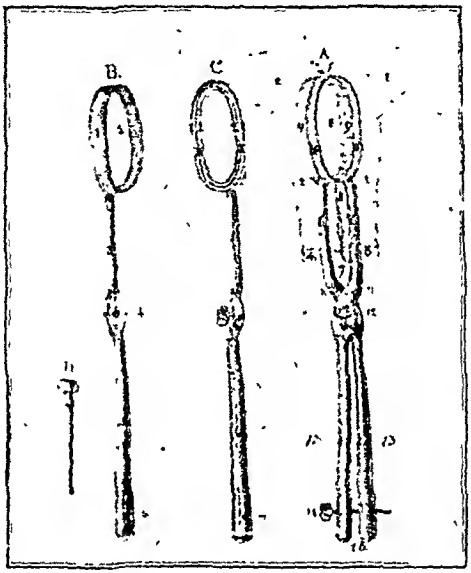



Fig. 14. Crushing clamp 1819.

After dividing the bowel as in the method of Jesset, invaginating and returning the lower end to the abdomen, he tied a wide glass tube into the upper divided end of the bowel. To this glass tube (the well-known Paul's Tube), was attached an india-rubber tube which guided the fæces into an antiseptic solution from the first, and so the abdominal wound was kept aseptic.

Although the intestinal crushing clamp is usually associated with the destruction of the spur of a double-barrelled colostomy as practised in the Paul-Mikulicz operation for colectomy, it is interesting to find that there are records that such a crushing clamp was used as long ago as 1819 for cure of an "intestinal fistula." Fig. 14 depicts the clamp, a description of which is given by Auguste Liotard in his "Dissertation sur le traitement dans anus contre nature," and which would do credit to some modern designs.

The importance of closing the lateral space or foramen between the colostomy and the parietes, in order to prevent small gut-obstruction, has been stressed by Rankin in America and by Gabriel in this country.(15)

In 1895 Harrison Cripps described a case of this type of obstruction following an inguinal colostomy. The operation for removal of the rectum is over two centuries old. Faget performed it in 1739. Lisfranc first successfully extirpated the rectum for cancer in 1826. In 1833 the great surgeon himself gave to the world a complete account of his operation and method, thus establishing the procedure as a surgical measure.(16)

The operation was a perineal excision without opening the peritoneum. The mortality was high, owing to the lack of aseptic technique. Nevertheless, for the next half-century, surgeons oscillated in their opinions between this operation and therapeutic measures. In the "System of Surgery," edited by Timothy Holmes, Assistant Surgeon to St. George's

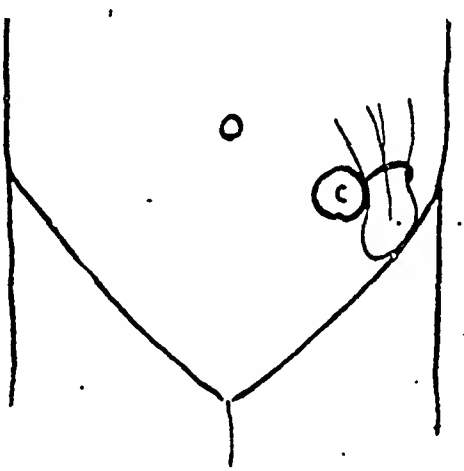



Fig. 15. Lateral space obstruction.

Hospital, dated 1864, there is an article on "Diseases of the Rectum" by H. Smith, Assistant Surgeon to King's College Hospital, in which appears the following statement:

> "Some surgeons were a few years since in the habit of performing excision of the lower part of the rectum when affected with cancer, but this proceeding must be looked upon both as barbarous and unscientific, and is now happily exploded from the catalogue of surgical operations."(17)

In 1877 Harrison Cripps, surgeon to St. Bartholomew's Hospital, was awarded the Jacksonian Prize for his essay entitled "The Possibility of Cure or Relief of Cancer of the Rectum by Excision." It was in some measure due to him that excision of the rectum for cancer became popularised and recognised as a legitimate and rational procedure in this country, despite the fact that Sir James Paget, who was regarded as

the greatest living authority of his day on cancer, had expressed the view that "The number of cases in which cancer does not recur after operation is not one in 500."(18) I will quote the words of Harrison Cripps: "There is scarcely an operation upon the human body which is not liable to be abused by the ignorant or enthusiastic, which, in the hands of a careful surgeon, would be of the utmost value to the sufferer. It requires the most careful selection to choose those cases of malignant rectal disease in which profit is likely to result from its removal."

How true were the observations of the pioneers of rectal surgery in their essentials when applied to modern methods!

Kocher, in 1875, and Harrison Cripps, about the same time, described a modified perineal excision.

The statistics given by Heuch of the practice of Professor Czerny for a period of six years are remarkable. Of 25 patients operated upon, only one died as the direct result of operation.(19)

In a paper read at the Société de Médicine of Lyone in May, 1884, M. Maurice Pollosson advocated the combination of laparo-colotomy with extirpation of rectal cancer. He selects the left iliac region for the colotomy. After the patient has recovered from the colotomy operation he then performs excision of the rectum as a perineal operation. In certain cases, however, he thinks that it might be advisable to proceed and extirpate the cancerous mass at once, after establishing the artificial anus. (How like our methods of more recent years.)

Allingham's operation was a perineal excision with preservation of the sphincter muscles. As a rule, however, it was found impossible to bring down the stump of the rectum to the anal skin. Quénu's technique was on similar lines.

In 1885, Paul Kraske, Professor of Surgery at Freiburg, devised a method by means of which it was possible for growths to be reached at a higher level. This approach was by excision of the coccyx and a portion of the sacrum. After resection of the growth, the ends of the bowel were either joined together by suturing, or the upper end was brought out at the top of the wound as a "sacral anus." In some cases, the rectum was completely removed and a sacral anus established. The first excision of the rectum that fell to my lot, when Resident Assistant Surgeon at St. Thomas's Hospital, in 1909, was on the lines of Kraske's operation, with the establishment of a sacral anus. Various modifications of Kraske's operation followed, with a view to obtaining better exposure of the growth. In these, larger portions of the sacrum were removed or else a bone-flap of a portion of the sacrum was fashioned and replaced after completion of the operation. The names of Bardenheur, Hockenegg, &c., are associated with these.

Frank Thomas Paul was born in 1851. He entered the Medical School of Guy's Hospital in 1869, went to Liverpool in 1875, and was elected Surgeon to the Royal Infirmary, Liverpool, in 1891. He was a pioneer

of the study of pathological histology, and was a consummate surgical craftsman. He anticipated Mikulicz by 10 years in his perfected method of colectomy.

In 1887 Dr. Alexander brought to Paul's notice the operation practised by a German surgeon, Dr. Paul Kraske of Freiburg, who had practised the operation in Germany. The introduction of the method of Kraske to this country is due to Dr. Alexander.

Fig. 16 Frank Thomas Paul.

*It is interesting to note that Ernest Miles, in his book on* "Rectal Surgery," states that: "The value of preliminary colostomy for preventing sepsis after an operation for excision of the rectum was not generally appreciated even as late as 1903." In a discussion at a meeting of the Medical Society of London, only one speaker was in favour of it.

Considerable progress has been made in the surgery of the rectum during the last 40 years.

Whilst bringing into the limelight the work of pioneers in the art of surgery, to whom all honour is due, one is liable to get a wrong perspective and not to apportion an adequate measure of praise and regard to the work of surgeons and research workers of more modern times.

In the surgery of cancer of the rectum of more recent years, the name of Ernest Miles stands out pre-eminently. Miles states in his well-known book on " Rectal Surgery " that in his early perineal excisions for carcinoma, the recurrence rate was 100 per cent. The operation was of a restricted type. By extending the scope of the operative procedure in successive series, he arrived at a removal which he stated was the most

Fig. 17. Ernest Miles.

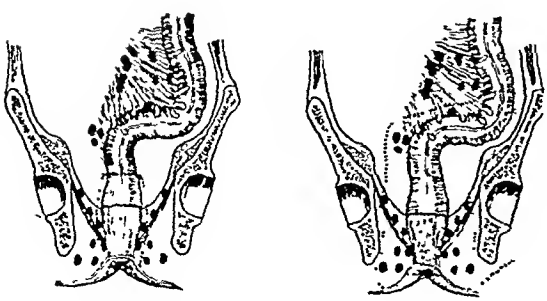


Fig. 18. Scope of perineal excision.

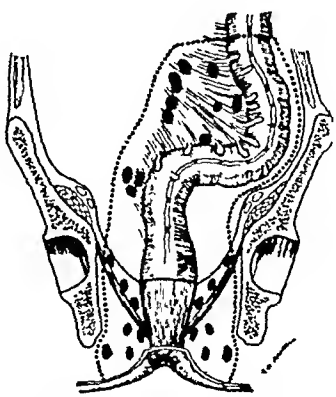


Fig. 19. Scope of perineo-abdominal excision.

complete that it was possible to carry out from the perineum. The recurrence rate with this operation was 94·4 per cent. Miles concluded that failure to prevent recurrence was due to the fact that tissues of the upward zone of spread already invaded, lay beyond the reach of any operation carried out solely from the perineum. He stated that these tissues, representing the axilla in cases of cancer of the breast, can be approached only through the abdomen. Hence the birth of his world famous " Abdomino-Perineal Excision " for cancer in 1907.

Miles(20) in an article published in 1920 states that " there are two main principles to be observed in the treatment of carcinoma of the rectum, and, indeed, of all cancers :

(1) The operation should be based on a knowledge of the demonstrable facts of pathology.
(2) The most extensive operation possible, in conformity with that knowledge, should be performed in all cases, no matter how small or early the local manifestations of the disease may seem to be."

Miles described *three* zones of lymphatic spread in cases of cancer of the rectum, namely, downward, lateral and upward.

Although all authorities are in agreement with the description given by Miles of the " upward spread," they do not all see eye to eye with his lateral and downward zones of spread. If his contentions were infallible, operations such as " Abdominal Resection," as described by Hartmann, or " Restorative Resection " in its various forms, would be unscientific and unjustifiable on pathological grounds.

The mortality from the abdomino-perineal operation remained high in the hands of most surgeons, and so in an attempt to counteract this, Lockhart-Mummery evolved his " perineal method of excision." He first performed this operation about the year 1914, but a description of it was first published in 1920.

In this he states that : " No operation for cancer can be considered satisfactory unless it can be employed with a reasonable degree of safety in cases where the patient is a bad subject." He also says : " The perineal operation is suitable for cases where the growth is at the anus or anywhere in the rectum proper, provided it is not fixed to important structures. It is not suitable for growths at or above the recto-sigmoidal junction."

In early cases of carcinoma recti, and especially with those situated in the lower rectum, the results have been striking. The perineal method of excision was usually performed in two stages, namely, colostomy, followed after an interval of 10 to 14 days by perineal excision.

There is much to be said for a thorough examination with a hand in the abdomen before deciding as to the operability or otherwise of a rectal cancer, and so planning one's method of procedure.

Hartmann, in an article published in the " Journal de Chirurgie"(21), stresses the importance of abdominal exploration in assessing operability

of a growth. Operability, in the majority of cases, cannot be determined without an abdominal exploration. A false impression may be gained by digital examination and sigmoidoscopy alone.

Sir Hugh Devine, in his well-known treatise on "Surgery of the Alimentary Track "(22) stresses the importance of passing a well-vaselined, gloved hand through a small incision, in order to explore the abdomen, before proceeding to more radical measures.

A two-stage operation may be considered advisable in removal of a growth by the abdomino-perineal route, especially in cases with marked intestinal obstruction.

In this connection certain details of technique have been advocated by Rankin, Lahey and others in order to try to minimise the danger of infection and peritonitis from the presence of the colostomy at the time of the second stage.(23)

Coffey's operation (24) is a form of two-stage abdomino-perineal excision which was practised extensively by certain surgeons both in this and other countries a few years ago.

The perineo-abdominal method of excision of the rectum was described by Grey Turner in an article in 1920.(25) He advocated a two-stage operation. The presence of the colostomy, however, provided a risk of sepsis and peritonitis when the second stage was performed. This risk proved a real one in cases treated at St. Mark's Hospital. For this reason, Gabriel devoted his attention to developing and improving the technique of perineo-abdominal excision in one stage, with a marked decrease in operative mortality.

Hartmann's method of abdominal resection for a growth in the upper rectum or recto-sigmoidal region, is pathologically sound, on the basis that the important upward zone of lymphatics is included in the parts removed. It has the advantage of leaving no perineal wound to heal.

The "extended Hartmann's operation," in which the rectum is divided low down in the pelvis, with closure of the distal stump, is in suitable cases advocated and practised by Mr. Hedley White and others.

The "Combined Synchronous Perineo-abdominal or Abdomino-perineal Excision" is a product of modern times.

The most important advance in the technique of "Combined Excision" is to place the patient in such a position that both the abdominal and perineal fields are exposed at the same time. It is then possible for a combined excision to be carried out by two surgeons working simultaneously and harmoniously. This method has been practised in recent years by Devine in Australia and Kirschner in Germany. At a meeting of the Association of Surgeons held in London a few years ago, Devine read a paper embodying this method of procedure, and also showed an admirable film in illustration. In this country Lloyd-Davies devised special crutches for the maintenance of a simultaneous "Lithotomy Trendelenberg Position." This position enables the perineal and abdominal fields to be exposed at the same time by an abdominal and

perineal surgeon working together. One great advantage is that there is no necessity to move the patient after he is once fixed in the required position, no matter what form of operation is decided upon, and so shock is minimised. The scope of the synchronous-combined method of operating has already been extended to other parts of the body. Hume has explored the possibilities of a synchronous-combined thoraco-abdominal operation for carcinoma of the lower end of the œsophagus, and in certain cases of total gastrectomy. By this combined action, growths which by other methods might be considered inoperable, may be successfully removed, together with other structures which may be involved in the cancerous mass.

Celsus stated that an essential qualification in a surgeon is an "intrepidity of mind, for want of which, some who are in other respects skilful operators, do frequently miscarry." If Celsus were alive to-day, he would rejoice to see the practical application of his aphorism as demonstrated by the successful removal of organs together with other structures infiltrated by malignant disease.

*Modern proctology* owes a great debt of gratitude to the work of Cuthbert Dukes. His researches into the paths of spread of cancer of the rectum, in which he has shown that the lymphatic spread is almost exclusively in an upward direction, along the course of the superior hæmorrhoidal vessels, as also his classification of "Cancer of the Rectum," on the basis of histology, and the practical value of histological grading of biopsy specimens, have gone far to revolutionise operative procedure and assessment of prognosis after operation.[26,27]

*Restorative Resection.*—On modern pathological grounds, in early cases with a low grade of malignancy as shown by histological examination of the biopsy specimen, it would seem justifiable to perform a restorative resection in certain picked cases.

In a discussion at the 88th Annual Meeting of the British Medical Association, held at Cambridge in June, 1920,[28] Professor Grey Turner summed up his remarks as follows:

> "The treatment of rectal cancer can never be considered satisfactory as long as the disease is so far advanced as to necessitate operations which leave an incontinent anus. Improvement can only come through much earlier diagnosis and consequent surgical treatment."

I have had the privilege of seeing some of Grey Turner's work and excellent results in certain cases of "Restorative Resection of the Rectum."

Devine is in favour of restorative resection in certain cases of growths in the recto-sigmoid region, preceded by a defunctioning transverse colostomy.[29]

Pannett described a restorative resection by sacral approach after the method of Goetze, as also by a combined abdominal and sacral approach. He states that there is much less liability to stricture formation after a restorative resection if no preliminary colostomy is performed.

I think there is enough evidence to show that in a certain percentage of picked cases, restorative resection is justifiable. Also when a permanent colostomy is refused by the patient. These remarks also apply to the abdomino-anal operation.

It is interesting to note the gradual improvement in operability rate of cases of carcinoma of the rectum due in part to increased experience and improvement in operative technique, but also to the determination and successful team-work with which these cases have been dealt.

At St. Mark's Hospital the average operability rate for the past three years was 80 per cent., and for the year 1947 it reached the astounding figure of 86 per cent.(30)

### Radium Treatment

Sir Charles Gordon-Watson in recording his experiences with interstitial radium in cases of carcinoma of the rectum, states that: "Prolonged experience has shown that the technical difficulties, in order to secure a perfect irradiation, are very great, and the results, despite a few brilliant successes, very uncertain, owing to the fact that adenocarcinomata vary considerably in radio-sensitivity."(31)

One of the greatest developments in the art and science of modern medicine is the cultivation of the team-spirit.

Moynihan, in his "Murphy Oration," stresses the importance of routine pre- and post-operative treatment in surgical procedure. Evolution and development have been gradual, but the value of these important adjuncts to surgery cannot be too greatly emphasised. One need only mention the preliminary cleansing of the bowel for several days prior to operation and the use of the sulpha drugs, notably sulphasuccidine and sulpha-guanidine, in the sterilisation of the colon and rectum, before excision or restorative resection.

Modern methods of anæsthesia, including spinal analgesia are: the use of curare to produce muscular relaxation, &c; the employment of gastric suction and drainage by means of a Ryle's Tube, as a post-operation measure, in cases of threatened ileus; pre- and post-operative transfusions, injection of penicillin, &c. Early rehabilitation treatment whilst in bed, such as breathing exercises to prevent chest complications, and exercises for the abdominal muscles and limbs to minimise the risk of venous stagnation with consequent thrombosis and the formation of emboli; early ambulation for similar reasons. These are some of the important developments in surgery of the present era, and are as applicable in the realms of proctology as to other parts of the body. Many lives have been saved as a result of their implementation.

### In Conclusion

One may liken the growth of any science, including that of proctology, to a shrub or tree, which starts in a small way, but gradually ripens and expands, till finally the full-grown product appears.

I do not wish, however, to give the impression that the "full-grown product" is yet in evidence, even in this year of Grace, 1948.

Towards the end of the 18th century, Percival Pott, in looking back after 50 years' practice, said:

> "Many and great are the improvements which the chirurgical art has received in the last fifty years; and many thanks are due to those who have contributed to them; but when we reflect how much still remains to be done, it should rather excite our industry than inflame our vanity."

Surgical craftsmanship is a progressive art. Improvements and new discoveries will continue to be revealed so long as this planet rotates in space. It was stated a few years ago by an eminent surgeon, whose name appears in the list of Bradshaw Lecturers, that: "Surgery had now reached its zenith, and that one must not expect any further progress in the art."

Even since the time when these profound words were uttered, the scope of surgery in various parts of the body has progressed with amazing rapidity.

To elaborate my simile, the fictitious tree has become more and more luxuriant. He would, indeed, be a bold man who attempted to predict finality in the growth of this tree, which is still throwing out its tender branches.

To illustrate my point: I would mention the progress made, and still being made, in the Surgery of the Chest, with which we in this College are proud to associate the name of Tudor Edwards. Also the progress being made in the Departments of Neuro-Surgery, Gastro-Intestinal Surgery and the Surgery of the Rectum. Remnants of some of the very early shoots are still evident on the parent trunk of the tree, which goes to emphasise the truth of the saying that "there is nothing new under the sun"—a maxim which I trust my investigations into the literature of the past have substantiated.

I would like to take this opportunity of expressing my thanks to Mr. W. R. Le Fanu, Librarian of the College, and to Mr. S. Wood, Assistant in the Library, for the great help they have given me.

## REFERENCES

1 MONTAGUE, J. F. (1929) The origin of rectal specialists and future of proctology.
2 HIPPOCRATES (1849) Works, trans by F. Adams. Sydenham society.
3 PAULUS ÆGINETA (1844-47) trans. by F. Adams. Sydenham society.
4 MILNE, J. S. (1907) *Surgical instruments in Greek and Roman times* Pl. 46.
5 ARDERNE, J. (1910) *Fistula in ano*, edif. D'Arcy Power.
6 HEISTER, L. (1770) *Institutions de chirurgie* **2**, 962.
7 HUNTER, J. Manuscript case-book, R.C.S., p. 441.
8 LISTER, J. (1867) The antiseptic principle in the practice of surgery. *Brit. Med. J.* **2**, 246.
9 PERRIN, W. S. (1931) *Proc. Roy. Soc. Med.* **25**, 338.

10 SALMON, F. (1832) *Lancet* 2, 238.
11 GORDON-WATSON, SIR C. (1934) *St. Bart's Hosp. J.* 41, 104.
12 MILLIGAN, E. T. C. (1934) *Lancet* 2, 1150; 1213.
13 SABATIER, R. B. (1774) *Mém. Ac. R. Chir., Paris* 5, 592.
14 DAVIES-COLLEY, J. N. C. (1885) *Lancet* 1, 522.
15 GABRIEL, W. B. (1928) *Proc. Roy. Soc. Med.* 21, 1433.
16 LISFRANC, J. (1833) *Mém. Ac. R. Méd., Paris* 3, 296.
17 HOLMES, T. (1864) *System of surgery* 4, 221.
18 PAGET, Sir J., quoted by Gordon-Watson, see No. 11.
19 HEUCK, G. (1883) *Arch. klin. Chir.* 29, 536.
20 MILES, W. E. (1920) *Brit. Med. J.* 2, 730.
21 HARTMAN, H. (1913) *J. Chir., Paris* 11, 693.
22 DEVINE, Sir H. (1940) *Surgery of the alimentary tract*: Bristol.
23 RANKIN, F. W. (1928) *Surg. Gynec. Obstet.* 46, 537.
24 COFFEY, R. C. (1922) *Ann. Surg.* 76, 500.
25 TURNER, G. G. (1920) *Brit. Med. J.* 2, 734..
26 DUKES, C. (1932) *J. Path. Bact.* 35, 323.
27 DUKES, C. (1948) Lettsomian lectures, Med. Soc. Lond.
28 TURNER, G. G. (1920) *Brit. Med. J.* 2, 734.
29 DEVINE, Sir H. (1934) *Austral. N.Z. J. Surg.* 3, 211.
30 ST. MARK'S HOSPITAL (1947) *Annual report* p. 32.
31 ST. MARK'S HOSPITAL (1935) *Collected papers* p. 400.

## SAYINGS OF THE GREAT

"One of the most valuable characteristics of the brain-working professions in Great Britain, and generally throughout the Anglo-Saxon world, is the claim which they have maintained to intellectual freedom in the exercise of their several vocations. This is a point secured by the remuneration of the professional 'consultant' not by salary, but by fees from a series of different clients. . . ."—*Sidney Webb* ("A Constitution for the Socialist Commonwealth of Great Britain").

"The existence in the professions of law, medicine, accountancy, architecture and engineering of a whole class of independent experts, not in the service of any person or corporate body, but ready to give responsible advice and assistance to a succession of clients, affords to the community the advantage of an independent check on the necessarily considerable influence of the secretarial bureaucracy and its own salaried technicians. . . ."—*Sidney Webb.*

" . . . it has been of the greatest value in Great Britain that the other members of each profession have continued in the position of unsalaried, independent consultants, called in only for specific purposes as required, and rendering their services in return for separate fees."—*Sidney Webb.*

---

Correction to previous number of the *Annals* in quotation from Osler, for "patience" read "patients."

# THE SIGNIFICANCE OF THE UNUSUAL IN THE PATHOLOGY OF INTESTINAL TUMOURS

Imperial Cancer Research Fund Lecture

delivered at the Royal College of Surgeons of England

on

23rd November, 1948

by

Cuthbert E. Dukes, O.B.E., M.D., Ch.B.

Director of the Research Laboratory, St. Mark's Hospital

I APPRECIATE THE HONOUR of being invited by the Imperial Cancer Research Fund to give this lecture on the pathology of intestinal tumours. Lest anyone should question the importance of the subject let me point out that the intestinal tract is one of the commonest sites of human cancer, that at present surgery offers the only reliable hope of cure and that surgical technique must be based on foundations of pathology.

I have chosen to speak to you about " the significance of the unusual " because a stage may be reached in the study of a subject when more can be learnt from the exception than from the rule. Another reason is because anything peculiar or exceptional in a disease treated surgically must be of practical interest to surgeons who want to know how often the rare occurrence is likely to be met with and under what circumstances. These are the questions I shall try to answer with regard to intestinal tumours which I have had a special opportunity of studying at St. Mark's Hospital.

Soon after I was appointed pathologist to this hospital 25 years ago I developed a method of examining operation specimens of intestinal cancer so as to learn as much as possible in each case about the origin, structure and spread of the growth. I have been fortunate in having been able to continue this work without interruption over a long period so that in more than 3,000 cases full details are now available as to the size and position of the primary tumour, the extent of local and venous spread and the number, size and position of all lymphatic metastases. These records have provided a clear picture of the usual paths of expansion and extension of intestinal tumours but they have also revealed a good deal that was surprising, contradictory and at first inexplicable. Further experience has clarified the significance of some of these strange phenomena even though all cannot be explained. I shall group this collection of curiosities under three headings " unusual appearance," " unusual histology " and " unusual methods of spread." This is a natural arrangement because some were noticed at first glance, others only by microscopic examination and others during dissection of the operation specimen.

## THE UNUSUAL IN APPEARANCE

The size of a tumour is a feature noticed at first glance, so let us consider *the significance of exceptionally large tumours.* We should of course expect a general relationship between the size of a tumour and the extent of its spread, so that the larger the tumour the worse the prognosis, and there is no doubt that this holds good for tumours of average dimensions, say between one and four inches in diameter. But does this direct relationship apply to the exceptionally large tumour, the monstrous trophy which the surgeon proudly exhibits at a scientific meeting? The answer is that it does not. Many of these exuberant neoplasms which extend widely over the surface possess little invasive tendency and are slow to metastasise, if indeed they do so at all (Fig. 1).

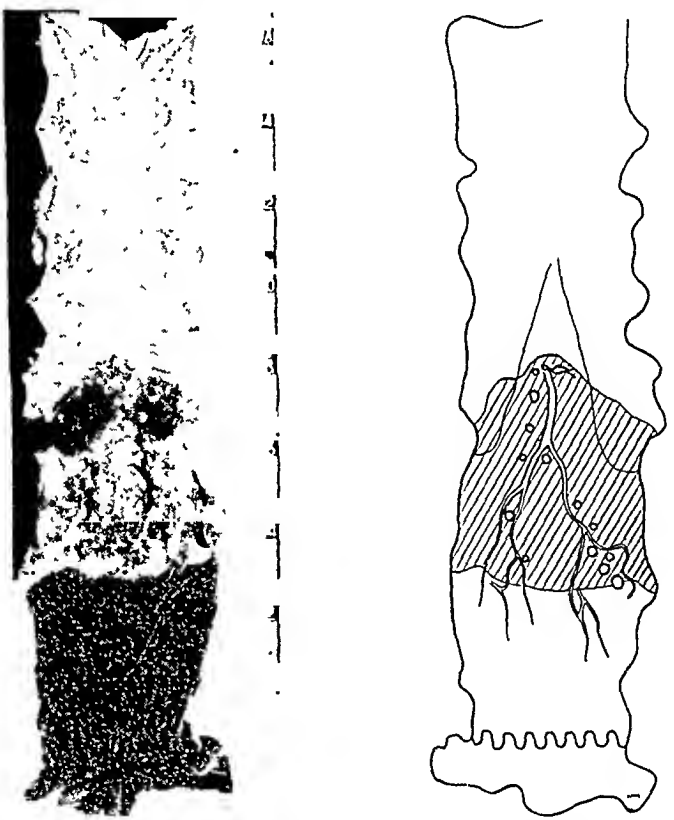
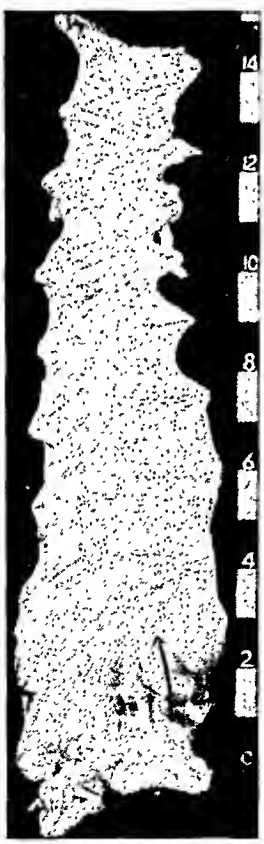


Fig. 1. Exceptionally large rectal cancer, but no lymphatic metastases.

Evidence in support of this is provided by a comparison of the incidence of lymphatic metastases in the two groups—the exceptionally large tumours and those of average diameter. In a consecutive series of 1,500 cases of rectal cancer I found 30 in which the primary tumour was more than four inches in diameter. The incidence of lymphatic metastases in these gigantic tumours was 10 per cent. lower than those of more modest

dimensions. So we reach the rather paradoxical conclusion that beyond a certain limit in size the larger the tumour the less the likelihood of metastases and, presumably, the better the prognosis.

Turning now from the monstrous to the tiny let us consider the significance of *unusually small tumours*. After what has been said about the comparatively good prognosis of exceptionally large tumours you will be prepared to hear that the innocent appearance of very small tumours may be deceptive. This is often so. Very small tumours, especially if deeply ulcerated, often prove to be anaplastic in character and are found to have given rise to widespread lymphatic metastases although there is little sign of local spread by direct continuity. Even more treacherous are the highly malignant growths which scarcely damage the surface yet spread like wildfire in the submucous lymphatics, an example of which is illustrated in Fig. 2.



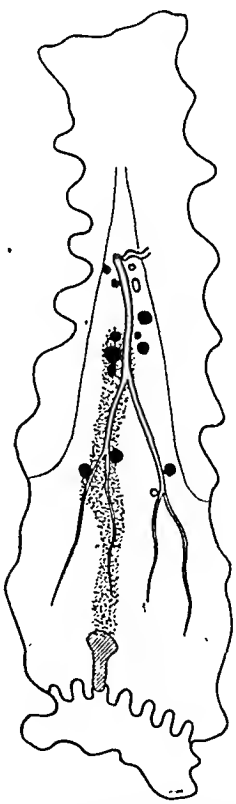



Fig. 2. Exceptionally small rectal carcinoma of lower third of rectum (marked by arrow) permeation of lymphatic trunks and 12 glandular metastases.

Here the only visible lesion was a narrow ridge (marked by an arrow in the photograph of the operation specimen) situated on the posterior quadrant of the lower third of the rectum. The tumour was scarcely

visible though it could be felt with the finger. Biopsy revealed an anaplastic carcinoma. A combined excision was carried out by Mr. W. B. Gabriel, and when the operation specimen was examined 12 lymphatic metastases were found in the hæmorrhoidal lymphatic glands and the intervening lymphatic trunks were found to be permeated with anaplastic carcinoma.

Fortunately not every tiny tumour is anaplastic in type. Sometimes a surgeon has the good luck to diagnose a small tumour of an average grade of malignancy still at an early stage of development and then, of course, the outlook is good. None the less our records at St. Mark's show that lymphatic metastases are more commonly found in tumours less than one inch in diameter than in those of average dimensions. There seems therefore to be a curious reversal of expectations at each extreme of size so that gigantic tumours are comparatively benign and very little ones often relatively malignant.

Now let us turn from the significance of unusual size to that of *numbers*. In most cases of intestinal cancer only one malignant tumour is found when the operation specimen is opened up and inspected, though multiple malignancy is by no means rare and would be recorded even more frequently if more of the intestinal tract could be inspected. We have found more than one focus of malignancy in nearly four per cent. of operation specimens when examining only the portion of the bowel removed by a combined excision of the rectum—about 20 inches on the average (Fig. 3).

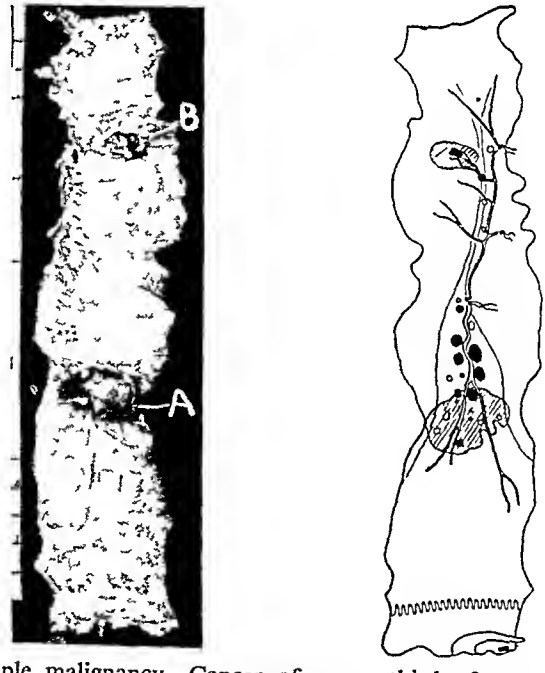



Fig. 3. Multiple malignancy. Cancer of upper third of rectum (A), and pelvic colon (B), lymphatic metastases from each.

Multiple malignancy is particularly common in association with *polyposis*, an unusual disease which certainly deserves a place in a survey such as this. The term " polyposis " is used to describe widespread epithelial proliferation of the intestinal mucosa leading to the formation of multiple adenomata. The tumours cover the whole surface of the colon and rectum varying greatly in size and appearance. The smaller ones are sessile, but the larger may be attached by broad strap-like stalks. The disease generally affects the large bowel only, not the small intestine or stomach. It is very liable to be followed by carcinoma and a focus of malignancy is to be suspected in any adenoma which is darker in colour and firmer in texture.

Clinicians distinguish two types of polyposis : a *familial* variety which manifests itself early in life and an *acquired* form appearing later and not familial in character. Both tend to malignancy but in the familial variety this is a greater danger because the polyps are more numerous and widespread. In most cases the distinction between the familial and acquired variety can only be made by a careful inquiry into the family history and by the examination of relatives. Obviously the first victim of the disease in a family will be regarded as an " acquired " case.

Polyposis is a rare disease and has been found in less than one per cent. of patients operated on for rectal cancer at St. Mark's Hospital. About half of these were found to be of the familial type. The distinctive character of familial polyposis is shown by the fact that the average age of polyposis patients operated on for rectal cancer has been only 32 years, whereas the average age for other cases of rectal cancer has been 57 years. Also the age of death from intestinal cancer in polyposis families has been earlier by 20 years than the average for intestinal cancer in the general population.

Lockhart-Mummery (1939) has suggested that polyposis is the result of a gene mutation, having as its consequence a more rapid growth of the intestinal mucosa, leading first to hyperplasia and later to adenoma formation. Whatever the nature of the inherited defect it seems to be handed on as a Mendelian dominant, being transmitted both by males and females. Possibly the disease may arise first of all by a chance mating of two individuals, each of whom is destined to die of cancer of the rectum. At any rate twice in the 20 families under observation at St. Mark's the disease is first recorded in a family in which both father and mother had died of cancer of the colon. Another of these families is of special interest because of the presence of twins in the second generation. Each of the twins developed polypi about the age of 30.

A polyposis family group is constantly changing its composition and the proportion of affected individuals varies from time to time. Some of the families included in our records at St. Mark's have been under observation more than 20 years and occasionally, though not often, we have witnessed the disease appear in an individual who at the first examination was recorded as unaffected. This occurred in the patient whose

operation specimen is illustrated in Fig. 4. This patient was first sigmoidoscoped at the age of 38 and found to be normal, but polypi were discovered when he was re-examined at the age of 44. Cancer of the colon developed at the age of 56 and was successfully treated by restorative resection. Cancer of the rectum appeared three years later and was treated by a combined operation. Within a few weeks a fresh focus of carcinoma broke out at the colostomy, and this unfortunate patient, having survived three major operations for removal of successive cancers of the intestine, died of secondaries 18 months after the last operation.

Fig. 4.

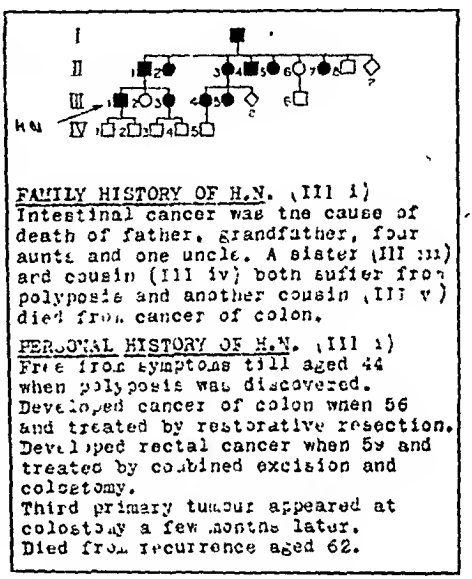



Fig. 5. Inheritance of intestinal cancer in polyposis family.

Fig. 4. Rectal cancer associated with family polyposis. Removed by perineo-abdominal excision.
(III i in pedigree chart.)

The family history of this patient is recorded in Fig. 5 (III i). Both his father and grandfather had died of rectal cancer as had five out of eight paternal uncles and aunts. A sister developed polyposis at 37 and two cousins are also known to be affected. These facts were known when the pedigree of this patient was first published by Lockhart-Mummery in 1925, but III i was represented then as unaffected. In 1939 Lockhart-Mummery and I brought the family history up to date and revised the

chart because III i had then developed polyposis. Now the tragic story has unfolded itself still further and the final entry must be made recording his death from intestinal cancer.

I am reminded that an American writer who has kept careful records of three polyposis families for several years has described tersely the vigilant attitude which must be adopted by the student of this disease. " A polyposis family group " he says " is an ever changing one and the chronicler must not lay aside his typewriter as the story must constantly be rewritten " (D. C. McKenney).

Polyposis is the last of the unusual features which I have grouped under the heading " Appearances." We now pass to unusual features revealed by the microscope, from the gross characters of intestinal tumours to details of their histology.

## THE UNUSUAL IN HISTOLOGY

No two tumours are exactly alike in microscopic structure but I have no intention of inflicting on you a long list of little peculiarities of doubtful significance. I shall mention only unusual features of a very striking character, most of them worthy to be described as " astonishing."

The first strange phenomenon is the association of *two totally dissimilar tumours*. Multiple malignant tumours are commonly of the same histological type but in the cases I am going to describe a carcinoma was associated in one instance with a melanoma, in another with a lymphosarcoma, in a third with a spindle cell sarcoma and a fourth with a carcinoid tumour.

In the case of carcinoma and melanoma the two tumours were widely separated, the adenocarcinoma being in the upper third of the rectum and the melanoma in the ano-rectal region. Each was typical in histology and each had caused lymphatic metastases, those from the adenocarcinoma being free from pigment, those from the melanoma packed with melanin.

The association of adenocarcinoma with lymphosarcoma occurred in a large protuberant tumour situated in the lower third of the rectum. The main bulk of the tumour had the histology of a lymphosarcoma but at its lower margin there was an abrupt change to well differentiated adenocarcinoma. The most probable explanation seemed to be that the sarcoma and carcinoma had at first developed separately from points in close proximity and later fused to form one tumour.

In the third example of double dissimilar malignancy a spindle cell sarcoma of the small intestine was associated with a rectal cancer and in the fourth a carcinoma was found in the cæcum and a carcinoid tumour in the small intestine. Carcinoid tumours of the appendix rarely give rise to metastases though in other parts of the intestine they may do so. In this case three lymphatic metastases were found near the carcinoid tumour but none in association with the adenocarcinoma of the cæcum.

Probably each of these four double dissimilar malignancies was only an accidental coincidence. They have been the only instances among 3,000 operation specimens.

The second unusual feature in the histology of intestinal tumours is the occurrence in the ano-rectal region of *mixed tumours* composed partly of squamous and partly of columnar epithelium. Most malignant tumours situated partly in the rectum and partly in the anal canal are found to be columnar cell carcinomas which have extended down from the rectum, though occasionally a squamous cell carcinoma of the anal canal is found trespassing up from below. Whether composed of columnar or squamous cells most ano-rectal tumours are of the same structure throughout but in a small proportion of cases (two-three per cent.) sections have shown the tumour to be mixed in its histology, the upper part being columnar cell and the lower squamous. When mixed tumours have given rise to lymphatic metastases they have been partly columnar and partly squamous in type.

No doubt mixed tumours are formed by the fusion of two foci of malignancy, one situated above and the other below the ano-rectal line.

*Leucoplakia* of the rectum is a very rare condition but I am going to mention a case in which it was so extensive as to be mistaken for malignant disease. The patient was an elderly man, an inmate for many years of a mental hospital. He was operated on for supposed rectal cancer and died a few hours later. This happened during the war at a time when medical services in London were disorganized and I was unable to obtain all the information one would have wished as to the patient's previous history.

Examination of the operation specimen, which arrived after the patient's decease, showed a diffuse papillary lesion encircling the rectal ampulla and spreading over four or five inches (Fig. 6). It was whitish in colour, stiff and unyielding in consistence and broken up by many cracks and fissures. The papilliferous part of the lesion ended abruptly about two inches above the ano-rectal line but the surface of the lower third of the rectum though smooth appeared to be covered by a greyish-white membrane. Microscopic examination showed an extreme degree of leucoplakia (Fig. 7). The mucous membrane of the lower two-thirds of the rectum had been completely replaced by stratified squamous epithelium which in the region of the ampulla had formed projecting horny nodules of keratin. There was no sign of carcinoma or of any other form of malignancy.

I must remind you that this patient had been detained for many years in a lunatic asylum. One of the problems of the inmates of these institutions is the safe custody of their personal possessions. During the day they can defend these from covetous neighbours but they have little protection against a thief who steals at night. Faced with these difficulties the mentally afflicted have been known to put the rectum to a use not intended by nature and to store their private treasures in its dark recesses each night, bringing them forth again each morning to the light of day.

You may have heard the story of the lunatic who was a great admirer of Napoleon and all day carried about a small bust of the Emperor which he returned each night to the safe keeping of his back passage. I have no evidence that the patient whose rectal lesion I have described was addicted to such practices but I cannot suggest any more likely cause for extensive squamous cell metaplasia.

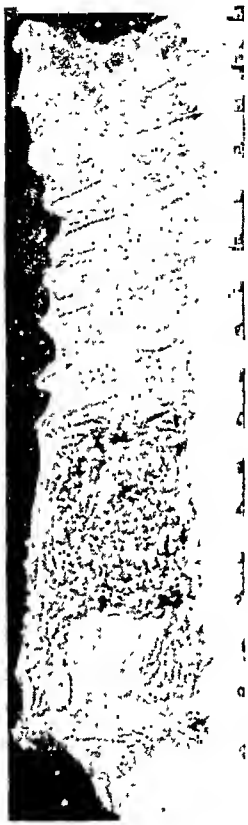


Fig. 6. Leucoplakia of rectum resembling carcinoma.

Fig. 7. Squamous cell metaplasia in rectal mucosa.

The fourth and last and equally unexpected peculiarity has been the occurrence of *ossification* in malignant tumours of the intestine. I have met with this four times—twice in the rectum, once in the pelvic colon and once in a recurrence from rectal cancer situated between the rectum and sacrum. In one case the ossified portion of the tumour was easily seen appearing as a hard greyish white mass projecting forwards from the centre. This was covered by little sharp spicules of bone. In the other three cases nothing unusual was visible on the surface but a grating sound was noticed when the tumour was cut open and bony spicules could be felt on the cut surface. The sections in each case showed a well differentiated adenocarcinoma with particles of bone in the stroma of the tumour.

The clinical history proved that these tumours had been present a long time : in one case certainly more than five years. The histological picture of a slowly growing adenocarcinoma of a low grade of malignancy fitted in well with this. There was very little local and no lymphatic spread. It looked therefore as though these tumours had reached a stationary phase and that ossification was occurring in an avascular region of the stroma as a result of connective tissue metaplasia.

Reference has already been made in passing to the possible surgical significance of each of these histological curiosities but they are not without significance also in relation to the problem of cancer in general. At any rate they are examples of the wonderful variety of tumour structure which is revealed when an intensive study is made of the pathology of any organ and they remind us also of the incalculable potentialities of the cancer cell, its adaptability and fixity of purpose—unpleasant attributes in an enemy whose progress we can do so little to thwart or retard.

## 3. UNUSUAL SPREAD OF INTESTINAL TUMOURS

Returning once more from the general to the particular let us consider the significance of some unusual methods of spread of intestinal tumours. I shall refer briefly to one unusual type of local spread, two of lymphatic and one of venous spread and my remarks will have a special bearing on the treatment of malignant tumours by local excision or restorative resection:

1. *Unusually Early Lymphatic Spread.*

In most cases of intestinal cancer the local intramural spread is a slow process and it is rare to find lymphatic metastases until direct continuity spread has extended to the peritoneum or other tissues surrounding the bowel. But in about two per cent. of all cases lymphatic spread may occur unusually early before the direct continuity spread has extended through the outer muscle coats. Exceptionally early lymphatic spread is most commonly found in anaplastic carcinomas of a high grade of malignancy and consequently has a poor prognosis.

2. *Discontinuous Upward Spread in Rectal Cancer.*

In rectal cancer the main direction of lymphatic drainage is upwards along the chain of glands accompanying the superior hæmorrhoidal vessels. The first glands to receive metastases are almost invariably those lying nearest to the primary tumour. After this the hæmorrhoidal glands are usually invaded in sequence from below upwards so that in an advanced case of cancer of the lower third or ampulla metastases form an unbroken chain extending from the regional group of glands to those situated at the point of ligature of the inferior mesenteric vessels. But from time to time a case is met with in which an isolated lymphatic metastasis is found high up in the upper hæmorrhoidal lymphatic glands though those at a lower level are free from deposits (Fig. 8). This is a rare phenomenon having been met with in only 2·4 per cent. of all cases.

It is probably due to an anatomical anomaly whereby some lymphatic trunks by-pass glands en route and pass directly upwards without halt to reach those in the recto-sigmoid region. Our follow-up records show that patients with discontinuous upward lymphatic spread have a relatively poor prognosis after operation.

3. *Downward Spread in Rectal Cancer.*

As already mentioned the first direction of lymphatic spread in rectal cancer seems always to be upwards but if the upward path is blocked by metastases or fibrosis then alternative routes may open up and metastases appear in unusual places. This is most likely to be encountered with tumours of the recto-sigmoid region as in the case illustrated in Fig. 9, in which several metastases were found below the primary growth

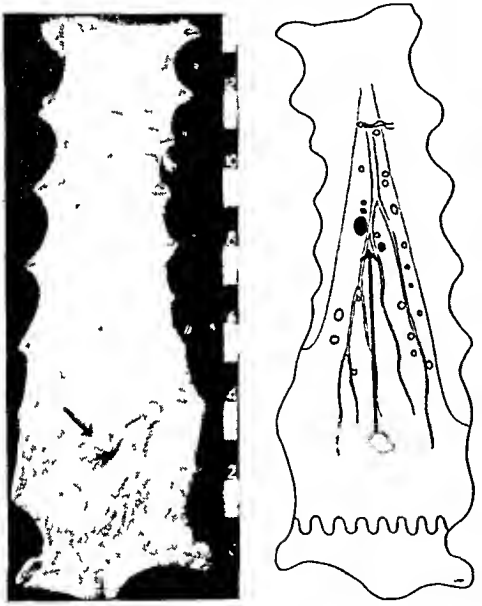


Fig 8. Discontinuous upward lymphatic spread in rectal cancer.

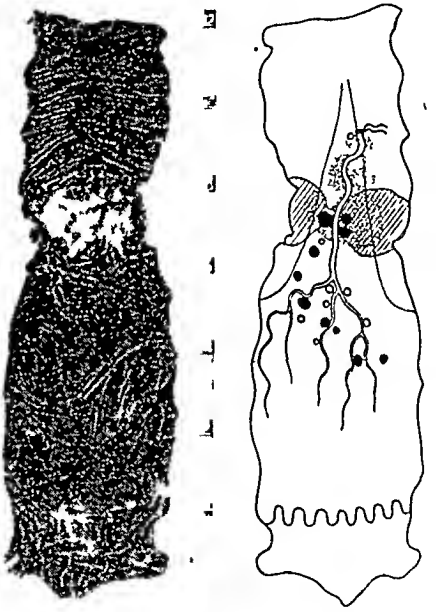


Fig. 9. Downward lymphatic spread in rectal cancer.

owing to the fact that the hæmorrhoidal blood vessels and lymphatics were buried in a solid deposit of carcinoma. This was a very exceptional, in fact, almost a unique case. Even minor degrees of downward lymphatic spread (resulting in an odd metastases or two below) are very rare, having been met with in only one per cent. of all cases of rectal cancer.

It must not be assumed that all downward spread in intestinal cancer is via lymphatic channels. Downward spread may occur in some cases by direct continuity, or in the lumen of the veins, or within a fistulous track or within the peritoneal cavity. It is possible also that infective material capable of giving rise to new foci of carcinoma may be carried down from above in the lumen of the intestine. Surgeons are apt to think

of downward spread only in terms of lymphatics but all possible routes have to be considered when seeking for an explanation of unexpected recurrences.

4. *Unusual Venous Spread.*

By the dissection of operation specimens evidence of extension within veins may be found in about 15 per cent. of all cases of intestinal cancer. Most commonly this intravenous spread preserves its connection with the primary tumour and is no more than a special form of direct continuity spread. It looks as if the malignant tumour, having found a path of least resistance, has pushed a root-like process along the lumen of a vein. Though this is the commonest form of venous spread occasionally a massive permeation of veins is found accompanied by thrombosis (Fig. 10).

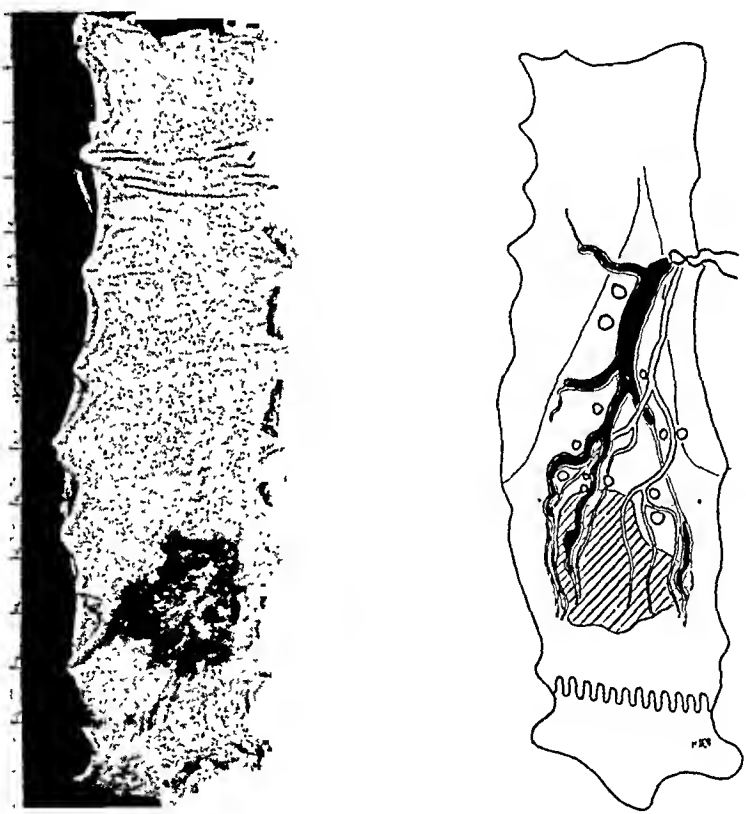


Fig. 10. Massive venous spread in rectal cancer. Survival for 11 years.

Patients with minor manifestations of venous spread, in which a plug of cancer cells firmly fixed to the primary tumour extends a short way along a vein, seem to have about the same chance as patients with a few isolated lymphatic metastases, that is to say that about one in three live

to celebrate the fifth anniversary of their operation. The rarer cases with massive venous permeation accompanied by thrombosis have a much worse prognosis. None the less some of our patients, who are known to have hepatic metastases, have remained in good health for many years and we are gradually collecting evidence that in some patients liver secondaries may remain latent for many years without impairing health. For instance, an abdominal operation was recently carried out at St. Mark's Hospital on a patient who, five-and-a-quarter years previously, had been treated for rectal cancer by a combined excision. There was now no sign of local recurrence in the pelvis, but the laparotomy revealed a metastasis from the former rectal cancer situated in the left lobe. This was successfully removed by Mr. O. V. Lloyd-Davies. It must have been there for more than five years.

The patient with massive spread in the superior hæmorrhoidal vein (whose operation specimen is illustrated in Fig. 10) is still alive and at work 11 years after his operation. No doubt most patients with hepatic metastases die within two or three years, but a few lucky ones survive. A combined clinical and pathological study of this small group may prove to be well worth while.

A start has already been made in this direction because some years ago I began to collect data about patients who had unexpectedly survived for more than five years in spite of evidence of very extensive spread of the disease, filing them under the label " Better than most," the phrase being derived from the Irish witticism—" One thing is as good as another and better than most." The records of patients who have done " better than most " are a reminder of the many unsolved problems in cancer immunity and it is fitting therefore that I should conclude this lecture on the significance of the unusual by referring to them in the hope that others may be stimulated to collect similar data and provoked to think about the subject.

But there are other reasons also why it is appropriate to end on this note. The disease which we have been considering in this detached and objective way is responsible for a very heavy burden of misery and suffering. We become well aware of this when we see malignant disease at close quarters and especially when it encroaches into the circle of our family or friends. Then it seems as though individually we can do exceedingly little. Our best hope seems to lie in organized cooperative effort and we turn with gratitude to acknowledge our indebtedness to organizations such as The Imperial Cancer Research Fund and The British Empire Cancer Campaign.

Mr. President and Members of the Council of The Imperial Cancer Research Fund—I began this lecture by thanking you for inviting me to give it and I must end by thanking all those who have helped me in the 25 years I have worked at St. Mark's Hospital. In the early years Mr. J. P. Lockhart-Mummery, then senior surgeon to the hospital, took a keen personal interest in the development of the laboratory and I owe a great

deal to this and to the support which he secured for me from The British Empire Cancer Campaign. I must refer also my obligation to another surgeon, Mr. L. E. C. Norbury, now Vice-President of this College, and to the present senior surgeon, Mr. W. B. Gabriel who started the follow-up department more than 20 years ago and has given it close personal supervision ever since. Undoubtedly my greatest obligation is to my senior laboratory assistant, Mr. H. J. R. Bussey, B.Sc. for his whole-hearted collaboration at all times and especially for his patient dissection of operation specimens, his care with records and his photographic skill, of which you have seen evidence. A most helpful assistant and loyal colleague.

I am under obligation to many others whom I cannot mention individually but perhaps I may be allowed to express my gratitude in the form of a parable. In the gardens of Lincoln's Inn, only a short distance from this venerable building there is a tulip tree which in 1948 has blossomed for the first time for 25 years. When I visited it in June I pondered on the long unnoticed activity which had proceeded year after year in root and leaf and stem, all in preparation for these brief blossoms. Similarly to-day I think back through the same span of years and pay grateful tribute to colleagues, assistants and friends, unrecorded but not unremembered.


REFERENCES TO POLYPOSIS

LOCKHART-MUMMERY, J. P. (1925) *Lancet* 1, 427.
LOCKHART-MUMMERY, J. P. and DUKES, C. E. (1939) *Lancet* 2, 586.
DUKES, C. E. (1947) *J. Clin. Path.* 1, 34.
MCKENNEY, D. C. (1936) *J. Amer. Med. Ass.* 107, 1871.
MCKENNEY, D. C. (1939) *Amer. J. Surg.* 46, 204.

REFERENCES TO SARCOMA AND MELANOMA

DUKES, C. E. and BUSSEY H. J. R. (1947) *Brit. J. Cancer* 1, 30.

REFERENCES TO MIXED TUMOURS

DUKES, C. E. (1946) *Proc. Roy. Soc. Med.* 39, 763.

REFERENCES TO OSSIFICATION IN RECTAL CANCER

DUKES, C. E. (1939) *Proc. Roy. Soc. Med.* 32, 1489.

REFERENCES TO SPREAD OF RECTAL CANCER

DUKES, C. E. (1932) *J. Path. Bact.* 35, 323.
DUKES, C. E. (1940) *J. Path. Bact.* 50, 527.
DUKES, C. E. (1944) *Proc. Roy. Soc. Med.* 37, 1.
DUKES, C. E. (1948) *Trans. Med. Soc. Lond.* (In the press).

# THE PATHOLOGICAL AND PHYSIOLOGICAL ASPECTS OF STERILE METABOLISM

Lecture delivered at the Royal College of Surgeons of England

on

24th November, 1948

by

Professor E. C. Dodds, M.V.O., F.R.C.P., M.R.C.S., F.R.S.
Courtauld Professor of Biochemistry in the University of London

THE EARLY ORGANIC CHEMISTS, who were interested in the structure of fats, found that, whereas pure fats could be completely saponified by boiling with an alkali such as potassium hydroxide, becoming converted into the potassium salt of the fatty acid, i.e., a soap, and glycerine, in certain animal and vegetable fats they found material which resisted saponification. This unsaponifiable material was found to be insoluble in water and to resist any attempt to convert it into a soluble soap.

Years of research on this unsaponifiable material showed that it consisted of substances which were ultimately called the *steroids*, and of which cholesterol is the most important, being present in all animal tissues.

The sterols contain hydrogen, carbon and oxygen, are soluble in organic solvents and are in some ways similar to fats, though far more complex. Through the work of Windaus (1932), of Rosenheim and King (1932, 1933), and of Wieland and Dane (1932) it was established that all sterols consist essentially of a condensed carbon ring structure in which the rings are arranged in what is known as the cyclo-penteno-phenanthrene ring system (Fig. 1).

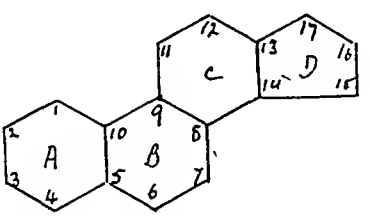



Fig. 1. Cyclo-penteno-phenanthrene.

Carbon atoms are numbered in accordance with accepted international custom. Groups such as hydroxyl (OH), methyl ($CH_3$) and ketone (=O) may be attached in various positions. Many of the sterols have hydroxyl groups or ketone groups at position 3, methyl groups at positions 10 and 13, and a variety of groups, or even a long side-chain at position 17.

It will be remembered from elementary organic chemistry that carbon atoms in a string can be joined together either by single bonds, in which

case two hydrogen atoms are attached to each carbon, or alternatively a hydrogen atom can be omitted from two adjacent carbon atoms and the valency satisfied by the appearance of a double bond. This, it will be remembered, is known as unsaturation. If we take six carbon atoms in a ring, these can be joined either by single bonds, in which case we have cyclo-hexane (Fig. 2), or we can have a maximum of three double bonds, in which case we have benzene (Fig. 3). Between these two extremes it is possible to have a six-membered ring with only one double bond. This is known as cyclo-hexene (Fig. 4).

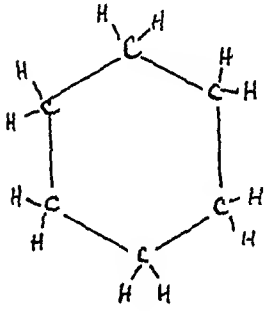


Fig. 2. Cyclo-hexane.

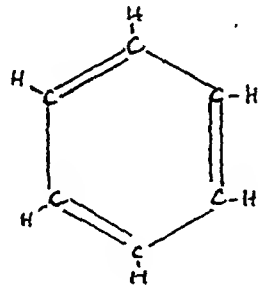


Fig. 3. Benzene.

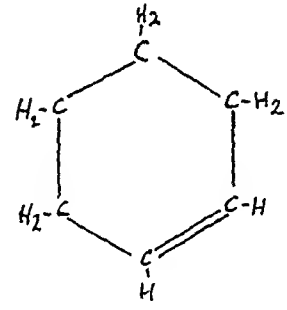


Fig. 4. Cyclo-hexene.

In the sterols one has the three six-membered rings and the five-membered ring joined together in the cyclo-penteno-phenanthrene grouping, as already stated. Now it is possible, theoretically, for the whole of this to be fully saturated, or hydrogenated, as we say. This means that all three six-membered rings and the one five-membered ring would consist of single bonds between the carbon atoms, the other valencies being satisfied by hydrogen. The sterols, and the derivatives which we are going to discuss, are not usually fully saturated compounds, and certain double bonds exist.

It is obvious that some form of nomenclature must be devised which will give the position of these double bonds, and also the position of the various hydroxyl, methyl and ketone groups which may be attached. A double bond is indicated by changing the " an " in the name of the parent hydrocarbon (e.g., hexane) to " en " (e.g., hexene), and in some cases the Greek letter $\Delta$ is introduced with the number of the carbon atom preceding the double bond. The presence of a hydroxyl group is indicated by the number of the carbon atom in front of the letters "ol", and a ketone group is indicated by the letters " one." The steroids of importance in the body are derivatives of the three hydrocarbons androstane, œstrane and pregnane (Figs. 5, 6 and 7). For instance, testosterone is a derivative of the hydrocarbon androstane. It contains a double bond between carbon atoms 4 and 5, a hydroxyl group at position 17, and a

ketone group at position 3. Its chemical name, therefore, is $\Delta^4$-androsten-17-ol-3-one.

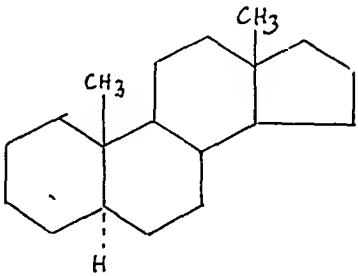



Fig. 5. Androstane.

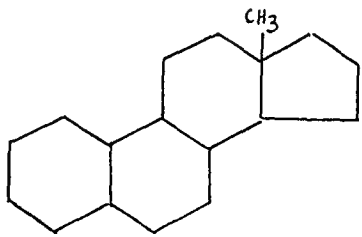



Fig. 6. Œstrane.

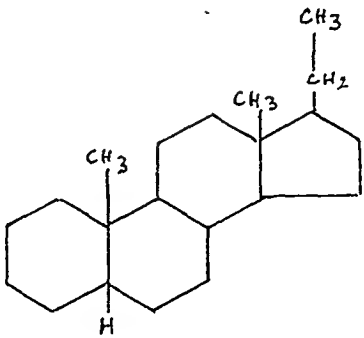



Fig. 7. Pregnane.

Further complications exist which may be briefly indicated. The steroids consist in the main of condensed carbon rings which are saturated. The rings of the cyclo-penteno-phenanthrene system are also lettered according to the scheme shown in Fig. 1. Thus rings A and B are completely saturated, and it is possible to have two forms of the rings themselves. It depends on what might be termed the "points" of the rings, i.e., carbon atoms 1 and 4 and 9 and 6. These "points" cannot be on the same plane owing to the fact that the four valencies of the carbon atom correspond to the points of a regular tetrahedron, and the "points" may be either above the plane of the paper or below. There can be two arrangements of this, in one of which one set of "points" is above the plane of the paper and one below. In this case the rings will present the appearance of a chair, as shown in the accompanying perspective diagram (Fig. 8), which is known as the trans-decalin arrangement, or more commonly as the allo variety. The cis-decalin or normal type, has the "points" of the rings both on the same side of the plane of the paper, suggesting the appearance of two beds (Fig. 9).

The question is still further complicated by the position of the angle methyl group in relation to the "points" of the rings, and the hydroxyl

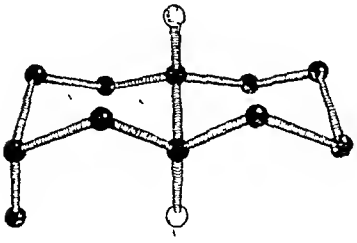


Fig. 8. Allo-type.

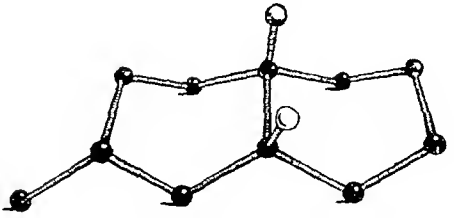


Fig. 9. Normal type.

group at position 3. Two varieties of allo form can exist. The first is the β variety, containing the hydroxyl group in the same plane as the methyl group and the hydrogen atom in the outside plane to both (Fig. 10).

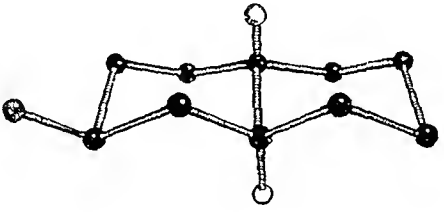


Fig. 10.

The question of stereoisomerism at this position is important when we come to consider the urinary excretion products. Those of the β configuration are precipitated by digitonin, whereas those of the α configuration are not, and this makes it possible to separate the α and β fractions.

It can be seen that the complexity of the rings is very great, and we have only dealt with rings A and B here. Stereoisomerism can occur in the other rings, and it is possible to postulate 32 isomers of, for instance, œstrone. Thus, it can be seen that the task facing the organic chemist is extremely difficult, since it is possible to synthesise a molecule having the correct formula, which is yet one of the 31 unnatural isomers.

The only other stereoisomeric problem that we need consider here is that of carbon atom 17. When the hydroxyl group is attached to the 17 carbon atom it is possible to have two isomerides, one in which the hydroxyl group is in the same plane as the angle methyl group on the 10 carbon atom, in which case the compound is said to be *cis*, and the second in which it is in the opposite plane, when it is termed *trans*.

## NORMAL STEROID METABOLISM

At the outset it must be stated that there are many gaps in our knowledge of this subject and that the actual process whereby the body produces these steroid derivatives from the sterol nucleus is not known. The origin of the body steroids is the metabolism of the various steroid

substances in the diet. In addition to cholesterol there is a vast number of phytosterols which presumably are converted into some common starting material for the synthesis of body steroids. The question as to whether the mammalian body can actually synthesise steroids is a debatable one, as it is impossible to elucidate the results of feeding experiments with sterol-free diets, owing to the very large stores of steroids in such places as the suprarenal, the liver and so forth. It is reasonable to suppose that the sterols of the food form the basis of the production of the body steroids.

The most important occurrences of steroids in the body are as follows:

(1) Cholesterol.
(2) The bile acids.
(3) The œstrogenic substances.
(4) The progestational substances.
(5) The androgenic substances.
(6) The adreno-cortical substances.
(7) Steroidal substances of unknown origin.

1. *Cholesterol* (Fig. 11).—This substance is one of the essential constituents of both animal and plant tissues. The largest quantities are present in the spinal cord, in the brain and in gallstones. A closely-related compound, coprosterol, is excreted in the fæces.

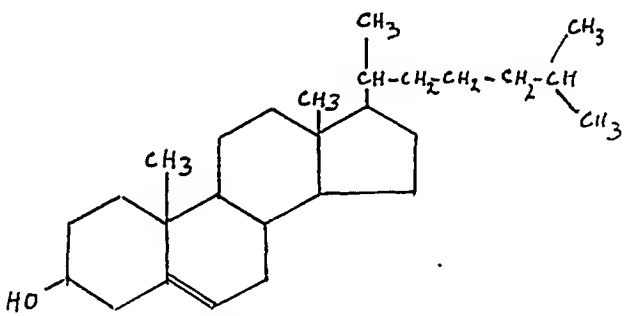



Fig. 11. Cholesterol.

2. *The Bile Acids* (Fig. 12).—These form a complex group of substances of the general type of formula similar to cholesterol. Human bile contains, in addition to considerable quantities of cholesterol, four acids, namely, cholic, deoxycholic, anthropo-deoxycholic and lithocholic acid. These acids are bound with certain amino acids and are present in the bile as bile salts, the most important of which are sodium taurocholate and sodium glycocholate. We are not concerned here with their physiological function in fat metabolism. It will be remembered that they are re-absorbed into the blood stream and are responsible for the secondary secretion of bile through their cholagogic action on the liver. They are

excreted again into the bile. This process was originally described by Schiff (1857) and was known to the older physiologists as Schiff's circulation of the bile salts. They occur in traces in the urine.

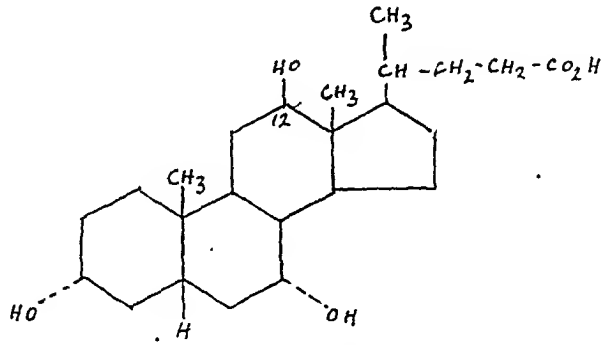



Fig. 12. Cholic acid.

3. *Œstrogenic Substances.*—Five œstrogenic substances have been isolated either from the urine of pregnancy or from ovarian tissue, namely, œstrone, œstriol, œstradiol, equilin and equilenin (Figs. 13 to 17). The latter two were isolated by Girard (1932) from the urine of pregnant mares, and do not occur in human urine. Œstradiol is found only in traces in the urine, but in considerable quantities in ovarian tissue. It is now considered to be the true œstrogenic hormone, being excreted in the urine mainly in the form of œstrone and œstriol.

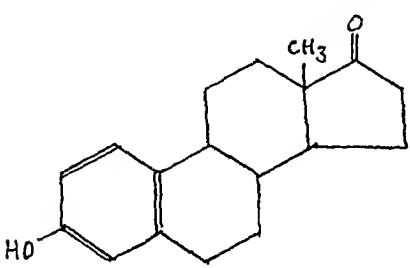



Fig. 13. Œstrone.

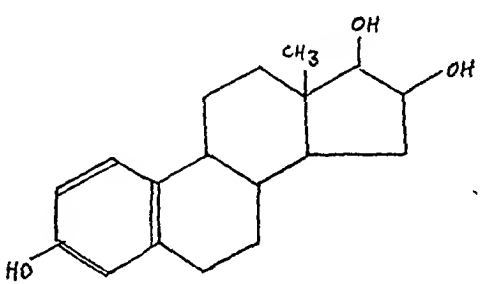



Fig. 14. Œstriol.

4. *Progestational Substances.*—Animal experiments indicated that it was very unlikely that all phases of ovarian activity could be ascribed to one type of hormone, namely, the œstrogenic. Active œstrogenic substances produce a certain development of the uterine mucosa, but not the characteristic glandular change in the endemetrium associated with full ovarian activity. By devising certain methods of standardisation, Corner and Allen (1929) demonstrated the presence of a progestational substance in ovarian extracts, and they showed that by the administration of injections of œstrongenic and progestational substances it was possible to reproduce the whole of the normal cycle. Intensive chemical work

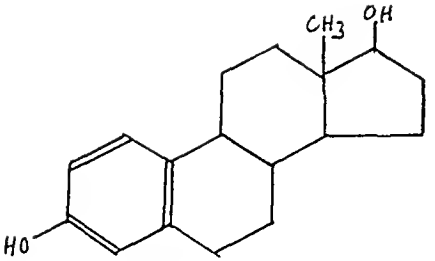



Fig. 15. Œstradiol.

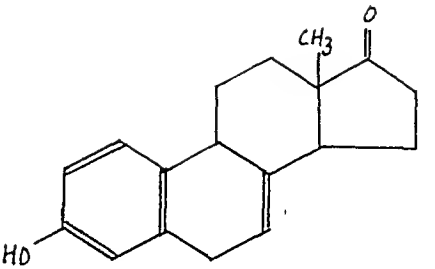



Fig. 16. Equilin.

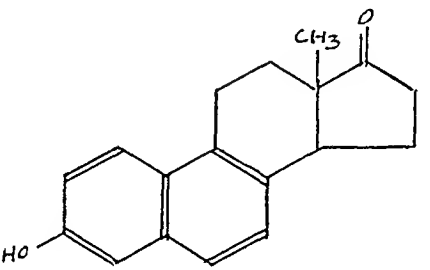



Fig. 17. Equilenin.

over a long period finally led to the characterisation of this substance which we now know as progesterone (Fig. 18) (Slotta *et al.*, 1934, Butenandt *et al.*, 1934, Allen and Wintersteiner, 1934, Hartman and Wettstein, 1935).

As can be seen from the formula, this is a ketonic substance and it has not been detected in the urine as such. A closely-allied substance has been isolated from the urine, namely, pregnanediol. Its relationship to progesterone can be seen in the accompanying diagram (Fig. 19) (Karrer, 1938), and it is regarded now as an end product of excretion.

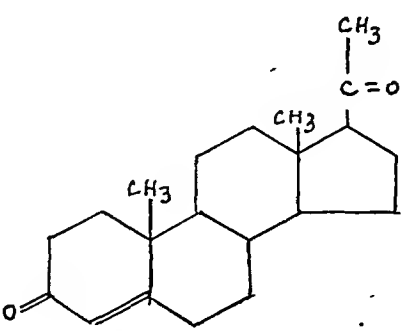



Fig. 18. Progesterone.

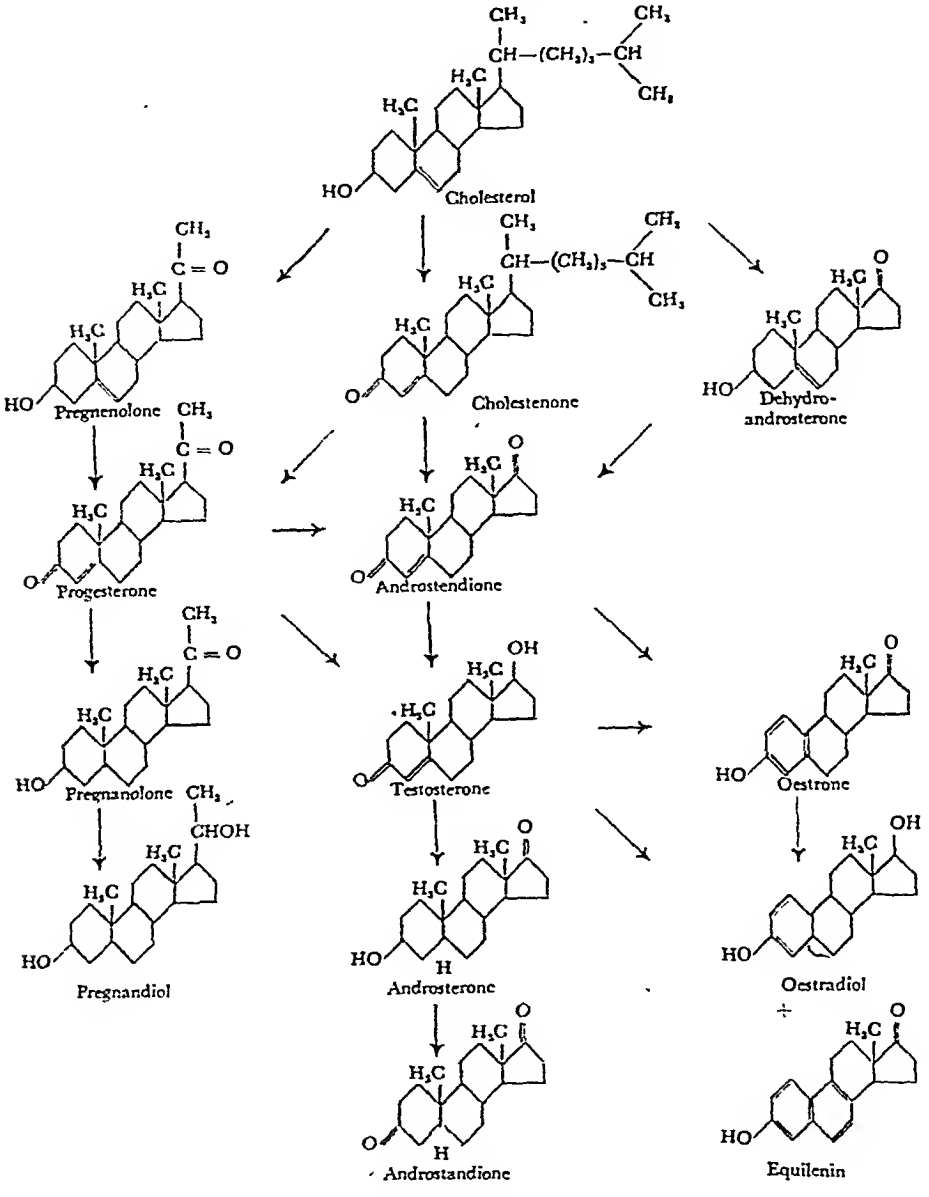



Fig. 19. (After Karrer.)

5. *Androgenic Substances.*—These have been mainly tested for their action in promoting the growth of the comb of the capon. The first active substances were obtained from the testes, but it was shown (Butenandt, 1934) that it was possible to extract from normal urine an androgenic substance. The constitution of this was eventually determined and it is known as androsterone (Fig. 20). Quantitatively the activity of pure androsterone was found insufficient to explain the activity of extracts of the testis, and eventually the actual androgen

produced by the testis was identified as testosterone (Fig. 21) (Laqueur *et al.*, 1935). Other androgenic substances are dehydroandrosterone (Fig. 22), dehydroisoandrosterone (Fig. 23), androstenedione (Fig. 24) and isoandrosterone (Fig. 25) These substances are excreted in normal urine in minute quantities. As will be seen later, certain of them are excreted in appreciable amounts in certain diseases of the endocrine glands.

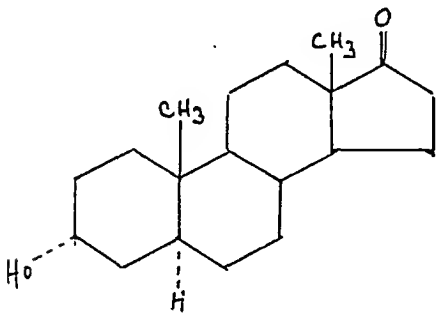



Fig. 20. Androsterone.

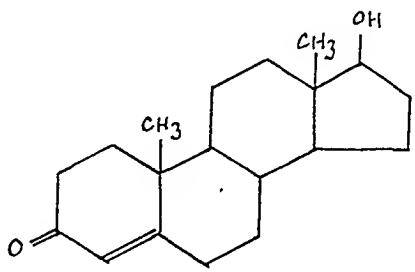



Fig. 21. Testosterone.

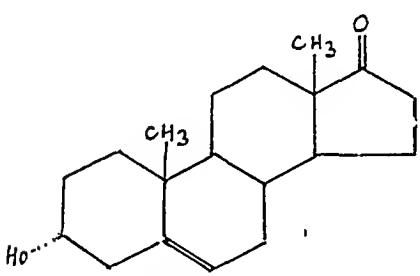



Fig. 22. Dehydroandrosterone.

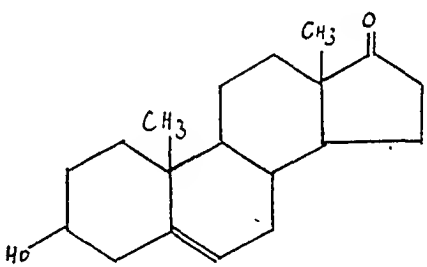



Fig. 23. Dehydroisoandrosterone.

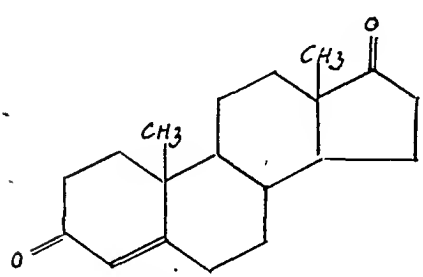



Fig. 24. Androstenedione.

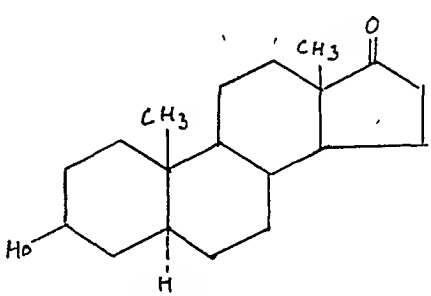



Fig. 25. Isoandrosterone.

6. *Adreno-Cortical Substances.*—The adrenal cortex enjoys the distinction of being the only tissue essential to life. Adrenalectomised animals can be maintained by the injection of a suitable extract, the first active one having been prepared by Swingle and Pfiffner (1931). Identification of the constituents of this active extract has been the subject of

vast and extensive work over many years. As the result of the labours of Kendall in the United States and Reichstein in Switzerland (see Kendall, 1934, Reichstein, 1936) and many others, a large number—at least 28—of steroidal substances have been isolated. Some of these are distinguished by having either a hydroxyl group or a ketone group attached to the 11 carbon atom. Such are corticosterone (Fig. 26) and 17-hydroxy-11-dehydro-corticosterone (Fig. 27).

A further substance, desoxy-corticosterone (Fig. 28) can be prepared artificially from cholesterol. This substance has also been isolated (Reichstein, 1938) from the adrenal cortex. As the production from cholesterol is a much easier process than the separation of the naturally-occurring substances, the compound most used in the treatment of Addison's disease is desoxycorticosterone. There are a great many other substances differing from one another in the distribution of double bonds in the molecule. They possess cortical activity in varying degrees.

In addition to steroids possessing corticoid activity there is a large number of other steroids produced by the adrenal cortex which possess feeble androgenic activity. Some of these will be referred to in the pathological section of these lectures.

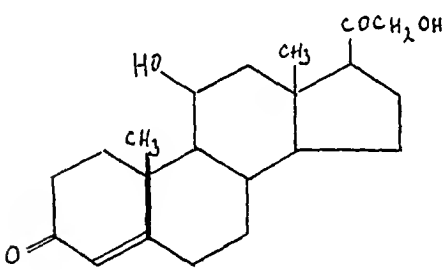



Fig. 26. Corticosterone.

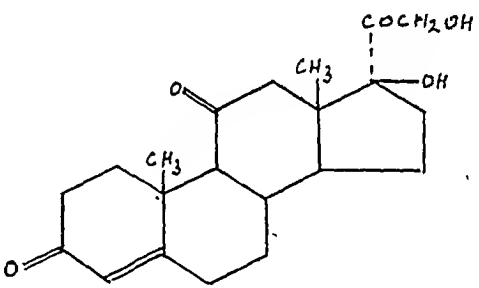



Fig. 27.
17-hydroxy-11-dehydro-corticosterone.

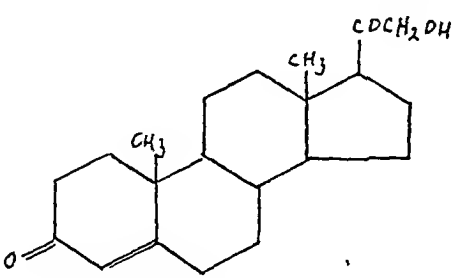



Fig. 28. Desoxycortico-sterone.

7. *Steroidal Substances of Unknown Origin.*—It is possible to isolate from the urine a whole series of substances of steroidal character, the origin of which is not known. Some of these substances possess multiple

biological activities. As an example can be quoted the synthetic substance pregninolone or ethinyl testosterone (Fig. 29). This substance is slightly androgenic, slightly œstrogenic and has very marked progestational activity. Some naturally-occurring steroids also possess this property.

The fact that a single substance can possess multiple activities from the biological point of view indicates the impossibility of estimating biologically œstradiol, testosterone, &c., in extracts of urine, blood, and so forth. Even though the potency could be determined accurately, provided sufficient animals were used, the result would defy interpretation, owing to the possible presence of steroids with multiple activities.

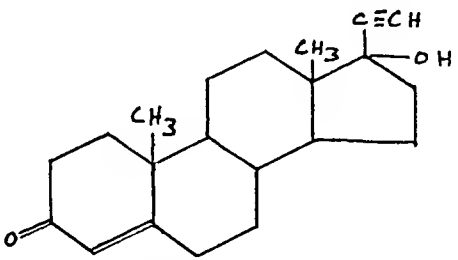


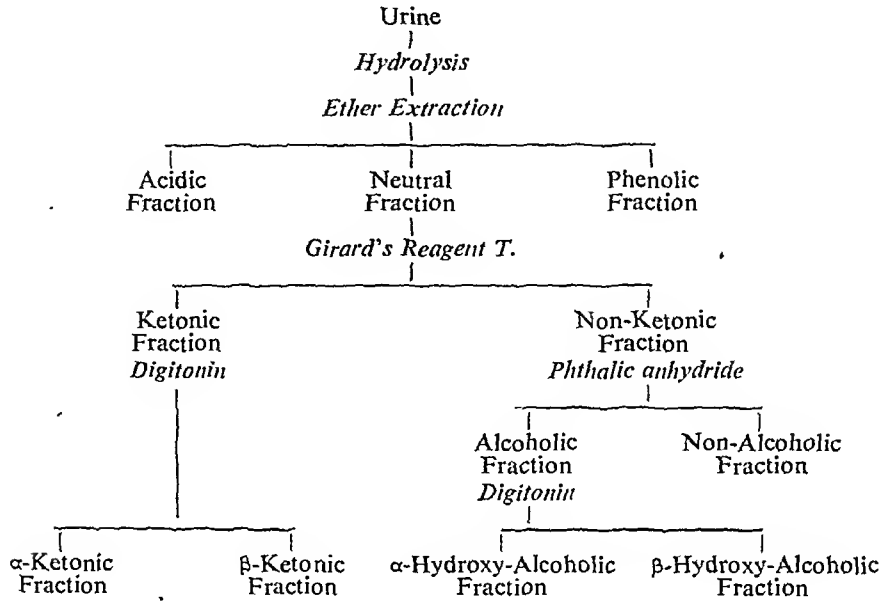

Fig. 29. Pregneninoline.

## METABOLISM OF STEROIDS, AS STUDIED BY URINE ANALYSIS

The only method of investigating steroid metabolism in the human subject is by an analysis of the urine. Large quantities of urine, at least a 24-hour specimen, are required, and the methods involve elaborate and cumbersome extractions and fractionations. Analysis of the blood for steroidal substances is for obvious reasons out of the question. The method of investigation by urine analysis is based mainly on the work of Dobriner and his colleagues (1942, 1944, 1948), and the following is a rough account of the type of method employed to-day.

As large a specimen of urine as possible is collected and is subjected to acid hydrolysis in order to liberate the free steroids from their conjugated products, such as glucuronides, sulphates, &c. After adequate hydrolysis the steroids are extracted with ether and the weight of material extracted here gives the total urinary steroids. This total extract is then separated into neutral, phenolic and acidic fractions. The neutral fraction is further divided into ketonic and non-ketonic fractions by the use of the well-known Girard T. reagent (Girard and Sandalesco, 1936). This compound unites with organic ketones, making them water-soluble, and so easily separable from the non-ketonic fraction. The ketonic fraction is still further subdivided by precipitation with digitonin into the α and β ketones. The non-ketonic fraction is also separated. Dobriner (1948) has set the procedure out in the form of a flow-sheet (Fig. 30), which shows the successive sub-divisions very clearly.

Fig. 30. Flow-sheet for extraction and separation of steroids from urine.




Dobriner and his colleagues then proceeded by chromatographic analysis to separate the actual constituents of these fractions and to characterise them by the ordinary methods of classical organic chemistry, and particularly by the application of modern methods such as infra-red spectrography. Amongst the individual compounds isolated, of which up to date 54 have been prepared, the following are some of the most interesting:

α—*Ketonic Fraction.*

*Normal Male and Female.*

Androsterone (also gonadectomised M and F, &c.).
3-α-hydroxyetiocholanone (also gonadectomised M and F, &c.).
$\Delta^{3,5}$-androstadienone (and also adrenal dysfunction).
$\Delta^{2}$ (or $^{3}$)-androstenone-17.
$\Delta^{11}$-androstenol-3-α-one-17.
Androstanedione-3-17.
Etiocholanedione-3-17 (trace only).
$\Delta^{9}$-androstenol-3-α-one-17.
Etiocholenol-3-α-dione-11-17.

*Normal Male only.*

Etiocholanol-3-α-one-17.
Androstenone acetate.

*Normal Female only.*

Androstanediol-3-α-11-β-17 (and also adrenal dysfunction).

*Pregnant Female.*

Allopregnanedione–3–20.
Allopregnanol–3–α–one–20.
Pregnanol–3–α–one–20 (and also adrenal dysfunction male and female).
17–isopregnanol–3–α–one–20.
Allopregnanediol–3–α–6–one–20.

*Adrenal Dysfunction Male and Female* (in addition to compounds quoted above).

Pregnanedione–3–20 (F).
Pregnanediol–3–α–17–α–one–20 (F).
$\Delta^4$–androstenedione–3–17 (M).

*Carcinoma of Breast and Prostate, Lymphatic Leukæmia, Cushing's Syndrome.*

$\Delta^9$–etiocholenol–3–α–one–17.

β—*Ketonic Fraction.*

*Normal Male and Female.*

Isoandrosterone (and also carcinoma and adrenal dysfunction).
Dehydroisoandrosterone (and also gonadectomised male and female and adrenal dysfunction).

*Pregnant Female.*

Allopregnanol–3–β–one–20.
$\Delta^2$–allopregnenone–20 (and also adrenal dysfunction).

*Non-Ketonic Fraction.*

α–*Hydroxy–Alcoholic Fraction.*

Pregnanediol (normal and pregnant female).
Androstanediol–3–α–17–α.

Compound E (Fig. 31) is very closely related in structure to the corticoid substances, as can be seen from a study of the formulæ and it is believed to play a part in carbohydrate metabolism. This substance appears to be present in many specimens of urine.

Androsterone, etiochólanolone (Fig. 32) and 11-hydroxy-androsterone have also been isolated from most specimens of urine.

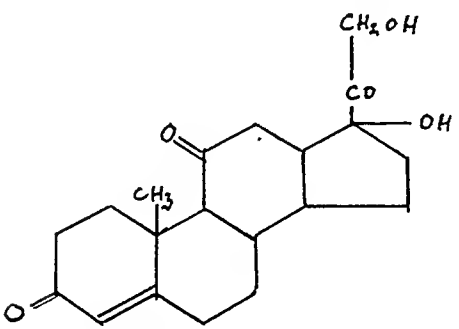



Fig. 31. " Compound E "

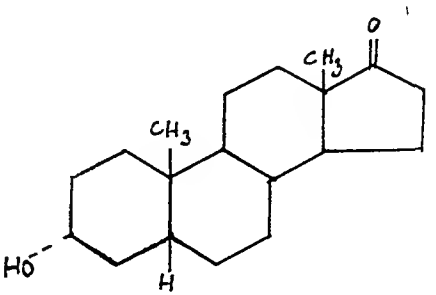



Fig. 32. Etiocholanolone

The steroid known as No. 18 is, perhaps, the most interesting. This is $\Delta^9$-etiocholenolone (Fig. 33). It is generally absent from normal urine and the urine of patients not suffering from cancer, but it appears to be present in considerable amount in cases of malignant disease. The workers are at present cautious in their statements, but there is a definite feeling that this substance may prove to be characteristic of malignant disease. It is thought to be produced by the adrenal cortex and it is hoped that future investigations will confirm that it is characteristic of cancer. There is an increase in other steroids in cancer, such as androsterone, $\Delta^9$-androstenolone, 11-keto-etiocholanolone and etiocholanolone. These increases, however, are not specific for cancer. If these observations can be confirmed in future work, then obviously a very important step has been taken in the whole question of cancer research.

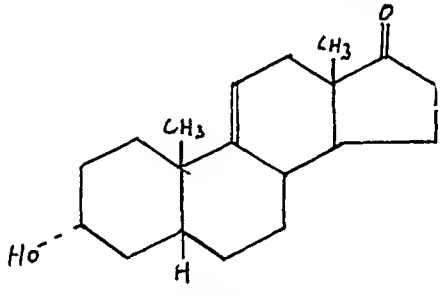



Fig. 33. $\Delta^9$-etiocholenolone.

Dobriner and his colleagues suggest that future work may show that some fundamental alteration in steroid metabolism of the suprarenal cortex may precede the actual establishment of malignancy. The presence of steroid 18 has definitely been detected in patients who subsequently developed cancer, and it has also been found in the urine of patients with Paget's disease, a condition definitely recognised by pathologists as being pre-malignant.

The investigations described above are, of course, far too elaborate to be undertaken by any ordinary routine department, requiring as they do a staff of very highly trained biochemists and physical and organic chemists. Recent work on the metabolism of androgens has been ably summarised by Dorfman (1948).

*Ordinary Routine Procedure.*—In most laboratories it is customary to estimate the total urinary steroids by ether extraction after previous hydrolysis, and then to determine the 17-ketosteroids in this fraction, either by colorimetric analysis or by polarographic analysis. Even these procedures are extremely laborious and again require the services of a well-trained biochemist.

It is natural that those cases exhibiting endocrine signs should have been investigated by the method of study of the urinary steroids. Generally speaking the cases fall under the following headings:
(1) Precocious puberty. (2) Virilism in females. (3) Feminism in males.

The conditions causing these symptoms are usually associated with tumours in the pituitary, ovary, testis or suprarenal. It must be pointed out at the outset that we have little exact knowledge of the excretory products in the conditions caused by these tumours, since most of the studies have been made on one or two cases, and it is of course unwise to generalise. As already pointed out, the work of Dobriner and his colleagues, when completed, will give the answer to these problems. In the meantime, it can be stated that most observations have been made on the four most important urinary steroids, namely androsterone, etiocholen-3-α-ol-17-one, dehydroisoandrosterone and isoandrosterone. The normal excretion of these substances has been given by Dobriner, from a limited number of cases, as follows: In normal young men the excretion of androsterone was found to vary between 5·2 and 6·6 mg. per day, and for etiocholanolone, 4·9 to 8·1 mg. per day. In the case of normal young women the excretion of both androsterone and etiocholanolone is about 3·0 mg. per day. Thus the androgenic contribution to the urine can be accounted for almost solely by androsterone, since the other substance is not androgenic. In terms of international capon units this amounts to 70 per day, but the dangers of the biological method of investigation have already been remarked upon.

Dehydroisoandrosterone and isoandrosterone are both β ketosteroids and are precipitated by digitonin. These substances form roughly 10 per cent. of the total ketosteroids, and, therefore, are excreted to the extent of 1·0 to 1·5 mg. per day in normal subjects. They are not very strongly androgenic and, therefore, would not be estimable by the biological method.

In castration there is a decrease in the total steroids and ketosteroids excreted, and in the castrated man the reduction is roughly to the same level as that of a normal woman (Hamburger, 1948).

In Addison's disease, again, there is a marked reduction in the excretion of ketosteroids, the level in females being zero or practically so. In experimental production of Addison's disease in the human subject Scott and Huggins found a marked reduction.

In Simmonds' disease the excretion is also very low, being below 5 mg. per day of total ketosteroids. This determination is of value in differentiating between cases of Simmonds' disease and anorexia nervosa, the clinical picture being very similar in these two conditions. In the latter the excretion of total ketosteroids is unaffected.

Adrenal tumours are frequently associated with premature puberty in children and masculinisation in addition. Callow (1936) was the first to isolate the androgens present in this condition, and demonstrated that dehydroisoandrosterone could be present in a large quantity, as much as 70 mg. per litre being obtained in one case. According to Callow, 70 per cent. of the androgenic activity is accounted for by this substance.

The actual origin of this compound is unknown, since the administration of other steroidal substances does not lead to an increased urinary excretion of dehydroisoandrosterone. It would be fairly safe, however, to conclude that its origin was in the suprarenal.

In Cushing's syndrome, when it is not associated with adrenal tumours, the steroidal excretion is normal, and the β-fraction again is normal. We can, therefore, say that the occurrence of an adrenal virilising tumour is associated with an increased excretion of the β-fraction of the 17-ketosteroids, of which dehydroisoandrosterone is the most important. It must, however, not be concluded from this that this substance is the only androgen excreted. Many other substances may contribute to the androgenic effect, of which androsterone is certainly one.

There are a very large series of papers which describe odd cases in which one or other of the steroidal substances mentioned have been found to be excreted in excess, but until these findings can be correlated, there is little point in discussing them here.

There has been no clear-cut evidence that steroidal substances with corticoid action are excreted in the urine. Various suggestions have been made that substances of unknown constitution with certain corticoid activities are excreted in some cases of Cushing's syndrome. Until they have actually been isolated and characterised little advantage can be gained from their consideration.

*Occurrence of Œstrogens in the Urine.*—Œstrogenic substances have been isolated from the urine of both masculinised women and feminised men. Determinations have been mainly made by the biological method, and as already pointed out, it is to be regretted that the position of œstrogen excretion cannot be satisfactorily considered at the present time.

*Pregnanediol*, which as stated above is an excretion product of progesterone, appears in the urine during the luteal phase of the menstrual cycle and in large amounts in pregnancy. In pregnancy the amounts are so large that they can easily be estimated. Marrian (1948) has now so refined the method of isolation of pregnanediol that it is now possible to assay the small amounts excreted during the luteal phase. Guterman (1944, 1945) has described a test for pregnancy based on the urinary excretion of pregnanediol, and has also claimed that by following the pregnanediol excretion during the early months of pregnancy it is possible to obtain warning of a threatened abortion, as in such cases there is a sudden drop in the excretion. Other workers, however, have not found this test very reliable and Bender (1948) considers that it can be applied to the diagnosis of a threatened abortion only in those cases where there is a deficiency of progesterone.

*Conclusions.*—Many readers of this involved story will wonder why so much trouble has been taken to explain what appears to be very little

from the point of view of practical medicine. To a critical reader it would appear that the investigations described are merely a very elaborate method of studying masculinisation and feminisation together with certain slight indications in the diagnosis of threatened abortion.

It must be admitted frankly that at the present stage the research workers have very little to offer to the practical clinician. The real point is whether this study of steroid excretion is the beginning of an entirely new chapter in the study of pathology. The American workers, for example at the Sloan-Kettering Institute, undoubtedly feel that the elaborate fractionation of urinary steroids will reveal a series of steroid excretion patterns, which, they hope, will be characteristic of certain diseases. It will be remembered that they feel already that there is a characteristic pattern in cancer and in Paget's disease, and possibly in certain cases of hypertension. They are hopeful that by extending their analyses they will be able to reveal characteristic patterns in other conditions and from this they hope that far-reaching conclusions will be drawn. For this reason it would appear to the writer essential that all those interested in the progress of medicine should attempt to understand this admittedly involved subject.

## REFERENCES


ALLEN, W. M., and WINTERSTEINER, O. (1934) *Science* **80**, 190.
BENDER, S. (1948) *Brit. Med. J.* **1**, 683.
BUTENANDT, A., and DANNENBAUM, H. (1934) *Z. Physiol. Chem.* **229**, 192.
BUTENANDT, A., and TSCHERNING, K. (1934) *Z. Physiol. Chem.* **229**, 167.
BUTENANDT, A., WESTPHAL, U. and HOHLWEG, W. (1934) *Z. Physiol. Chem.* **227**, 84.
CALLOW, R. K. (1936) *Chem. Ind.* **55**, 1030.
CORNER, G. W., and ALLEN, W. M. (1929) *Amer. J. Physiol.* **88**, 326.
DAVID, K., DINGEMANSE, J., FREUD, E., and LAQUEUR, E. (1935) *Z. Physiol. Chem.* **233**, 281.
DOBRINER, K., GORDON, E., RHOADS, C. P., LIEBERMAN, S., and FIESER, L. F. (1942) *Science* **95**, 534.
DOBRINER, K., LIEBERMAN, S., and RHOADS, C. P. (1948) *J. Biol. Chem.* **172**, 241.
DOBRINER, K., LIEBERMAN, S., RHOADS, C. P., JONES, R. N., WILLIAMS, V. Z., and BARNES, R. B. (1948) *J. Biol. Chem.* **172**, 297.
DOBRINER, K., RHOADS, C. P., LIEBERMAN, S., HILL, B. R., and FIESER, L. F. (1944) *Science* **99**, 494.
DODDS, E. C. (1939) Cantor Lectures, Royal Society of Arts, London.
DORFMAN, R. I. (1948) Metabolism of Androgens, *Recent Advances in Hormone Research*, **2**, 179. Academic Press, New York.
GIRARD, A., and SANDALESCO, G. (1936) *Helv. Chim. Acta* **19**, 1095.
GIRARD. A., SANDALESCO, G., FRIDENSON, A., GODEFROY, C., and RUTGERS, J. J. (1932) *C. r. Acad. d. Sc.* **194**, 1020.
GIRARD, A., SANDALESCO, G., FRIDENSON, A., and RUTGERS, J. J. (1932) *C. r. Acad. d. Sc.*, **194**, 909.
GUTERMAN, H. S. (1944) *J. Clin. Endocrinol.* **4**, 262; (1945) *Ibid.* **5**, 407.
HAMBURGER, C. (1948) *Acta Endocrinol.* **1**, 19.
HARTMAN, M. and WETTSTEIN, A. (1935) *Helv. Chim. Acta* **17**, 878, 1365.
KARRER, P. (1938) *Organic Chemistry.* Trans. by A. J. Mee. Elsevier, Amsterdam.
KENDALL, E. C., MASON, H. L., MCKENZIE, B. F., MYERS, C. S., and KOELSCHE, G. A. (1934) *Proc. Staff Meet. Mayo Clin.* **9**, 245.
LIEBERMAN, S., DOBRINER, K., HILL, B. R., FIESER, L. F., and RHOADS, C. P. (1948) *J. Biol. Chem.* **172**, 263.
REICHSTEIN, T. (1936) *Helv. Chim. Acta* **19**, 29.
REICHSTEIN, T. and EUW, J. v. (1938) *Helv. Chim. Acta* **21**, 1197.
ROSENHEIM, O., and KING, H. (1932) *J. Soc. Chem. Ind.* **51**, 954; (1933) *Ibid.* **52**, 299.

SCHIFF (1857) *Untersuch. z. Naturl. d. Mensch. u.d. Tiere*, 2, 345.
SLOTTA, K. H., RUSCHIG, H., and FELS, E. (1934) *Ber.* 67, 1270, 1624.
SOMERVILLE, I. F., GOUGH, NANCY and MARRIAN, G. F. (1948) *J. Endocrinol.* 5, 247.
SWINGLE, W. W., and PFIFFNER, J. J. (1931) *Amer. J. Physiol.* 98, 144.
WIELAND, H., and DANE, E. (1932) *Z. Physiol. Chem.* 210, 268.
WINDAUS, A. (1932) *Z. Physiol. Chem.* 213, 147.

## SIBERT FORREST COWELL

SIBERT FORREST COWELL, Secretary of the College from 1901 to 1934, died on 13th January, 1949, at the age of 85.

Second son of Thomas William Cowell, M.R.C.S., of Piccadilly, Forrest Cowell was a Queen's Scholar of Westminster and scholar of University College, Oxford, where he graduated B.A. in 1886, and M.A. in 1911. He joined the staff of the College as Assistant Secretary in 1887 to fill the vacancy caused by the appointment of the late Sir Frederic Hallett as the first Secretary of the Examining Board in England.

He made the work of the College almost the only interest in his life and soon acquired an accurate and intimate knowledge of its affairs. He served the College he loved with a single-minded devotion, and his work received the particular commendation of the Council on three occasions, the Centenary Celebrations in 1900, successful negotiations with the Inland Revenue authorities in 1910, and finally when he laid down his Office. Although of a quiet and retiring disposition he made many friends by his kindly nature and unfailing courtesy.

After his retirement in 1934, he continued to live in West Kensington until enemy action forced a retreat to St. Albans, where he spent the last years of his life.

## THE RESTORATION AND DEVELOPMENT FUND

READERS OF THE *Annals* will have seen in the daily Press, and in the weekly medical journals, the announcement of Lord Nuffield's wonderful gift to the College. This gift is for purposes additional to the original plans for restoration and development. It will include residential quarters so that graduate students, research workers, teachers and visitors will be able to live in a collegiate atmosphere and to meet each other socially as well as in the class rooms and laboratories. Details of the plans of the Nuffield College will be published at an early date.

Notable gifts since the last report include one hundred pounds from the staffs of the hospitals of Canton and area, as a mark of friendship and esteem from this group of hospitals in South China ; and a donation of fifty guineas from Mr. F. C. Ormerod.

Over £192,000 has now been subscribed towards the £250,000 required for the original plans for the restoration and development of the College. On John Hunter's birthday (14th February), those Fellows of the College who have not yet subscribed will receive a letter from the President once more asking them to support their College in its hour of need.

## "OBSERVABLES" AT THE ROYAL COLLEGE OF SURGEONS

### 14. THE ROWLANDSON WATER-COLOURS

THE COLLEGE is fortunate in possessing four drawings by Thomas Rowlandson, all of them of topical interest. The Editorial Committee thought that subscribers to the *Annals* would be interested to possess copies of these drawings so they have been reproduced in monochrome in the present number, each of them on a separate sheet.

The subjects of the College drawings are hardly suitable for the drawing-room, so would not fetch the thousands of pounds which Rowlandson's drawings of more decorative subjects have recently fetched in the sale-room.

Thomas Rowlandson (1756-1827), who was famous in his lifetime as a caricaturist, has been recognized in recent years as a great artist. What interested him was the everyday life of his fellow creatures, their humours, their pomposities and antics, their foibles and obscenities, their vanities and crudities. His sense of design was highly developed, and his best work stands comparison with that of any water-colourist. His work is usually executed in outline with the reed-pen and delicately washed in colour. He had a rare dexterity of touch and fertility of imagination. Rowlandson illustrated works by Goldsmith, Smollett and Sterne. His "Tours of Dr. Syntax" with verses by William Combe were published by Ackermann—

"Dr. Syntax in search of the picturesque,"
"Dr. Syntax in search of consolation,"
and "Dr. Syntax in search of a wife."

In "The Microcosm of London" with Pugin's photographic accuracy and his feeling for the subtle lighting of fine architecture, we have Rowlandson's humanity, his sharp observation and magical knowledge of what makes an English crowd.

"The Dissecting Room" is reputed to represent Dr. William Hunter demonstrating at the Great Windmill Street School. This house is still standing and now forms the stage door and dressing rooms of the Lyric Theatre. It was presented to the College by Dr. William Tiffin Iliffe.

"Transplanting of Teeth" was presented by J. Strathan.

"The Irish Giant" is well known to all visitors to the College, for his skeleton is in the Museum—and thereby hangs a tale! The drawing was in the Hunterian Collection.

"John Heaviside Lecturing" was presented by Mr. H. J. Joel to the President, by whom it was given to the College. John Heaviside was a member of the Council of the College from 1800 to 1828, before which he had been a member of the Company of Surgeons from 1793 to 1800.

W-J.

Cruikshank
Howison

William Hunter

Hewson

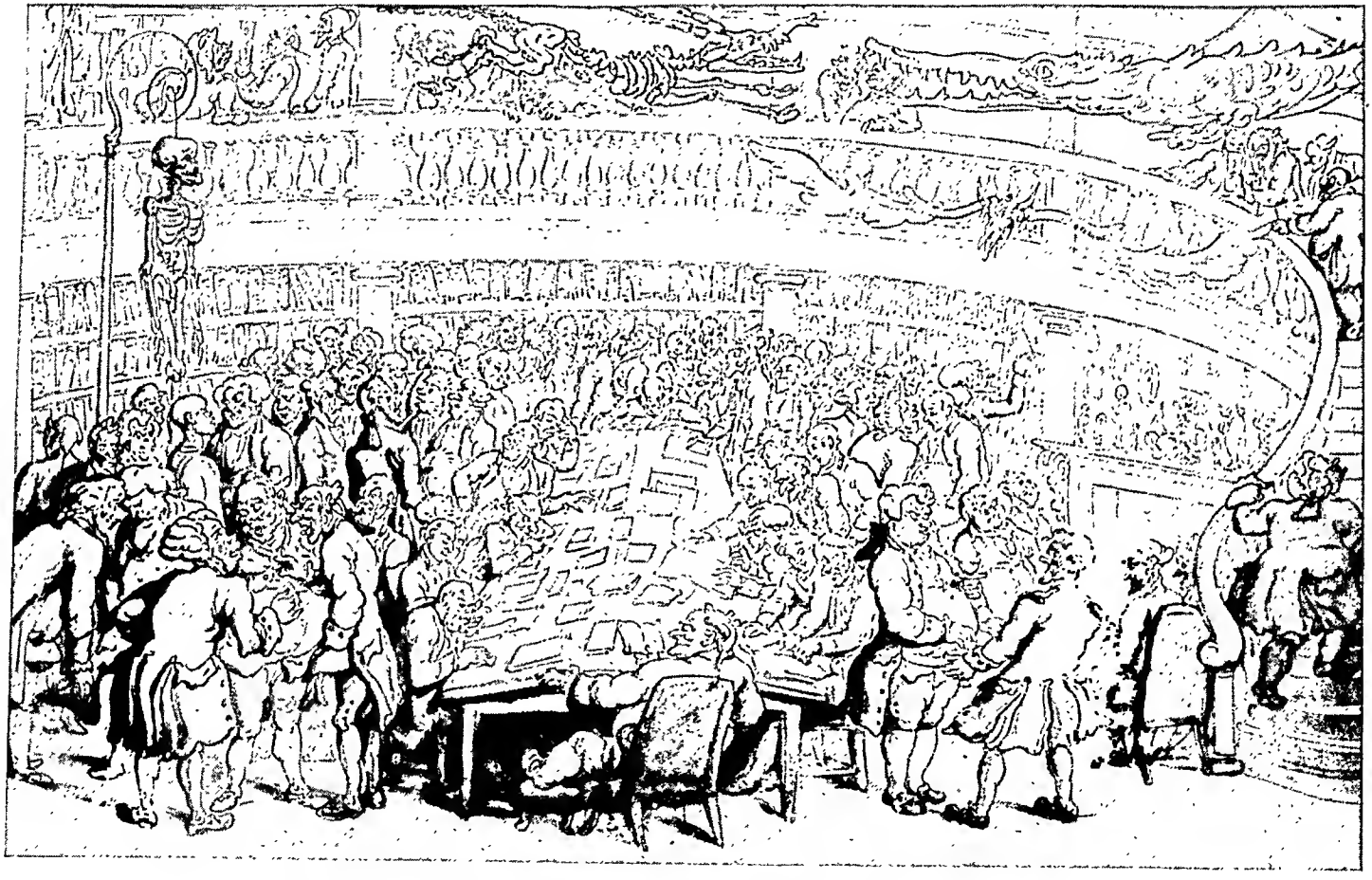
Tobias Smollett

The Dissecting Room—by Rowlandson.

Among others are: William Pitcairn, Matthew Baillie, Howe, Sheldon and Camper.

Transplanting of Teeth—by Rowlandson.

O'Brien, The Irish Giant—by Rowlandson.



JOHN HEAVISIDE (1748-1828) Lecturing at Surgeons' Hall—by Rowlandson.

# THE LIBRARY

## JOHN HUNTER'S WRITINGS

### INTRODUCTION TO AN EXHIBITION

---

WAS JOHN HUNTER illiterate? Was he so busy with his knife, as anatomist and surgeon, that he had no time to read or write? A glance at the long series of his writings will convince that this calumny ought to have been dead a hundred and fifty years.

His first published writing was a report on his experiments of 1758-59—his 31st year—to demonstrate *absorption by veins*; it appears in his elder brother's *Medical Commentaries*, 1762, and begins appropriately: ANIMAL FIRST Experiment I. Four years later came his first appearance in the Royal Society's *Philosophical Transactions*, 5 June 1766: an anatomical supplement to John Ellis's *Account of an amphibious bipes.*

Hunter's first book, *The natural history of the human teeth*, was published in 1771; the College owns the original manuscript and the splendid red-chalk drawings by Jan van Rymsdyk, an artist who had already worked for William Hunter and later drew the series of *the development of the egg and the progress and peculiarities of the chick*, which was published by the College long after John Hunter's death. This series of drawings is in the collection of *Hunterian Drawings.*

These drawings were considered a part of the Museum which they illustrate, and were not sold with Hunter's library and pictures. They were mounted, probably by the care of William Clift, in four large albums, and have always been a chief treasure of the College Library. Hunter did not himself draw, but he employed several first-rate artists, some of them, William Bell for instance, being also skilled anatomists. Similarly he wrote little with his own hand, preferring to dictate to a secretary and afterwards correct the manuscript. Owing to the burning of his papers much of the writing left unpublished at his death survives only in Clift's transcripts, but enough originals remain to show that most was in secretaries' hands. The manuscripts of his books on *The Teeth* and *The Venereal Disease*, both in the library, are in this category, as are several *original museum catalogues*; only one slim volume of these catalogues is wholly in Hunter's own writing.

The great series of his contributions to the Royal Society runs in the *Philosophical Transactions* from 1772 to 1792. (The original drafts preserved at the Royal Society were written out by his secretaries.) The series begins with his famous paper, *On the digestion of the stomach after death*, and reaches its climax in the years 1786-87, when he contributed four papers, as well as publishing two books—*The Venereal Disease*, and *The Animal Œconomy*—from his private press. The last of these four papers is the 75-page monograph, *On the structure and œconomy of Whales*, the summary of a lifetime's work, which was followed five years later by a similar masterly summary of his *Observations on Bees* (1792). In this paper Hunter says that he was not concerned to publish the anatomical description of a species, but to explain the life-function of a class.

Of whales he had dissected a large number of a variety of species. How did he come by them? When a whale, with its calf, was stranded in the Bristol Channel, he wrote to Edward Jenner to send it to him in London. How did you send a whale across England in the 1770s? Hunter's letters to Jenner give precise instructions, and after its arrival he wrote that it was being dissected and drawn. Magnificent drawings of various dissected organs of whales are in the collection, besides those of the whole animals.

This orientation of his research lies behind most of his important papers, such as *Receptacles of air in Birds*, 1774, the two papers on *Heat of Animals and Vegetables*, 1777, and the *Organ of hearing in fish*, 1782. When the new strange animals were first sent home from Australia, Hunter was the one man in Europe equipped to classify them by their anatomical affinities. He was fortunately applied to, and his *Description of the kangaroo* and other Australian animals was published, with the first pictures of them, in White's *Journal of a voyage to New South Wales*, 1790.

After the College had taken charge of the Museum there was some necessary delay in its organization, but in the 1830s, 40 years after Hunter's death, Richard Owen published the great five-volume *Catalogue of the Physiological series of Comparative Anatomy*. This more than anything else established the scientific prestige of the College, as well as setting Owen in the front rank of anatomists while still a young man. In these volumes many of Hunter's writings and drawings were published for the first time, his work, for instance, on *the growth of bone* and on *the growth of feathers*. Here, too, is reproduced a beautiful drawing of a hedgehog dissected. Hunter was almost obsessed with hedgehogs; the unexplained physiology of hibernation fascinated him. He kept them in his garden at Earls Court, and had frequent replenishments sent up alive by Jenner from the west country. Owen continued to glean from Hunter's manuscripts and published numerous fragments and short studies, culminating in the two volumes of *Essays and observations*, 1861.

During the whole period of his biological studies Hunter was also writing surgical papers: on *Cæsarian section* in the Medical Observations and Inquiries by a Society of Physicians, 1774, on *Recovery of the apparently drowned* in the Philosophical Transactions, 1776, on *The operation for popliteal aneurism*, 1786, and on *Introsusception*, 1789, for his own Society for the improvement of medical and chirurgical knowledge, founded in 1783, a select society of leading practitioners. In 1785 he founded another society, of large membership, for students, the Lyceum medicum Londinense. This published no journal, but a copy of its *Rules*, with the list of members and an account of its library, is in the College, as also the *Prize essay* for 1788, by Everard Home, both printed at Hunter's private press by "John Richardson, printer to the Society." The Essay has on its title page a picture of the prize medal bearing the portraits of John Hunter and George Fordyce, patrons of the Lyceum medicum. Hunter's writings concluded with his greatest book, *The Blood, inflammation and gunshot wounds*, published in 1794, just after his death, but originally inspired by his war experience of more than 30 years before.

---

An exhibition of John Hunter's manuscripts, drawings and printed books was shown in the Council Room at a meeting of the Osler Club on December 10, 1948.

## MONTHLY DINNERS

Monthly dinners are held in the College on the second Wednesday of each month. The following are entitled to attend with their guests: All Diplomates and students of the College, and Members of the Associations linked to the College through the Joint Secretariat. It is not necessarily intended that guests should be members of the medical profession.

The dinners will be at 7 p.m. on the following Wednesdays: March 9, April 6, May 11, June 8, and July 13, 1949. There is an inclusive charge of £1 5s. (including drinks), which must be sent with the application to the Assistant Secretary at least a week before the date of the dinner. The dress is Lounge Suit or Uniform.

## DIARY FOR FEBRUARY (15th-28th)

| | | | |
|---|---|---|---|
| Tues. | 15 | 5.00 | Dr. J. Douglas Robertson—Metabolism Disorders in Thyroid Disease. |
| | | 6.15 | Prof. John Kirk—Fascial Planes of the Neck. |
| Wed. | 16 | 5.00 | Prof. G. Payling Wright—Repair of Connective Tissues. |
| | | 6.15 | Dr. R. L. Waterfield—Blood—Physiological Aspect. |
| Thur. | 17 | 5.00 | Prof. J. G. Bonnin—Hunterian Lecture—Diastasis of the Tibio-Fibular Syndesmosis.* |
| Fri. | 18 | 5.00 | Dr. J. Douglas Robertson—Calcium Metabolism. |
| | | 6.15 | Mr. A. Bulleid—The Application of Bacteriology to Dental Procedure. |
| Mon. | 21 | 5.00 | Prof. D. F. Ellison Nash—Hunterian Lecture—The Development of Micturition Control.* |
| | | 5.00 | Prof. H. H. Stones—The Diagnosis and Treatment of Pathological Conditions of the Pulp (Part 1). |
| | | 6.15 | Dr. Geoffrey Organe—Anæsthesia in relation to Dental Surgery. |
| Tues. | 22 | 5.00 | Prof. H. H. Stones—The Diagnosis and Treatment of Pathological Conditions of the Pulp (Part 2). |
| | | 6.15 | Mr. V. Zachary Cope—Actinomycosis. |
| Wed. | 23 | 5.00 | Prof. W. S. Lewin—Hunterian Lecture—Acute Subdural and Extradural Hæmatoma in Closed Head Injuries. |
| Thur. | 24 | 5.00 | Prof. R. Roaf—Hunterian Lecture—The Treatment of Residual Disability following Injuries of the Peripheral Nerves of the Upper Extremity.* |
| | | 5.00 | Mr. H. T. Roper-Hall—Therapeutics in Dental Surgery. |
| | | 6.15 | Mr. R. J. McNeill Love—Cervical Glands in relation to Dental Surgery. |
| Mon. | 28 | 5.00 | Prof. R. A. Russell Taylor—Hunterian Lecture—The Ætiology, Pathology, Diagnosis and Treatment of Acute Pancreatitis: a Review of 110 Cases.* |
| | | 5.00 | Mr. Myles L. Formby—Sinusitis and Allied Problems in relation to Dental Surgery. |
| | | 6.15 | Dr. A. C. Roxburgh—Skin Diseases in relation to Dental Surgery. |

## DIARY FOR MARCH

| | | | |
|---|---|---|---|
| Tues. | 1 | 5.00 | Mr. Philip H. Mitchiner—Arnott Demonstration.* |
| | | 5.00 | Prof. A. A. Moncrieff—Children's Diseases in relation to Dental Surgery. |
| | | 6.15 | Sir Charles Symonds—Facial Pain. |
| Thur. | 3 | 5.00 | Pre-Medical Examination begins. |
| | | 3.45 | Mr. R. J. Last—Arnott Demonstration.* |
| | | 5.00 | Dr. A. H. Harkness—Non-Gonococcal Urethritis. |
| | | 5.00 | Mr. A. L. D'Abreu—Chest Diseases in relation to Dental Surgery. |
| | | 6.15 | Dr. E. W. Fish—Treatment of Advanced Parodontal Disease. |
| Mon. | 7 | 5.00 | Dr. F. S. Gorrill—Arnott Demonstration.* |
| | | 5.00 | Mr. P. Rae Shepherd—Fractures of the Mandible (Part 1). |
| | | 6.15 | Mr. J. H. Doggart—Diseases of the Eye in relation to Dental Surgery. |

* Not part of courses.

| | | | |
|---|---|---|---|
| Tues. | 8 | 5.00 | MR. R. BATTLE—Free Skin Grafting : Methods and Application. |
| | | 5.00 | MR. P. RAE SHEPHERD—Fractures of the Mandible (Part 2). |
| | | 6.15 | SIR CECIL WAKELEY—The Nerves of the Face and their Surgical Significance. |
| Wed. | 9 | 5.00 | MR. PHILIP H. MITCHINER—Arnott Demonstration.* |
| | | 5.00 | MR. H. L. HARDWICK—Gingivitis. |
| | | 6.15 | MR. RAINSFORD MOWLEM—Non-union Fractures of the Mandible. |
| | | 7.00 | Monthly Dinner for Fellows, Members and Licentiates (see page 125). |
| Thur. | 10 | | D.T.M. & H. Examination begins. |
| | | 5.00 | MR. W. HYNES—Skin Flaps : Indications and Technique. |
| Fri. | 11 | | D.C.H. Examination begins. |
| | | 5.00 | MR. J. SCOTT TOUGH—Bone Cartilage and Fascia Transplants. |
| Mon. | 14 | 5.00 | MR. A. C. BUCHAN—Burns and their Early Treatment. |
| Tues. | 15 | 5.00 | MR. J. P. REIDY—Cleft Lip and Palate Repair. |
| | | 5.00 | MR. B. W. FICKLING—The Approach to Oral Surgical Diagnosis. |
| | | 6.15 | PROF. M. A. RUSHTON—Endocrine Effects on Teeth and Jaws. |
| Thur. | 17 | | First Membership Examination begins. |
| | | 5.00 | MR. D. N. MATTHEWS—Congenital Lesions of Skin and Subcutaneous Tissues. |
| | | 5.00 | PROF. POMFRET KILNER—Facial Repair. |
| | | 6.15 | PROF. M. A. RUSHTON—Hyperplastic Jaw Lesions. |
| Fri. | 18 | | L.D.S. Examination (General and Special Anatomy and Physiology) begins. |
| | | 5.00 | MR. M. OLDFIELD—Fractures of the Facial Skeleton. |
| | | 5.00 | MR. E. S. LEE—Cancer of the Mouth. |
| | | 6.15 | MR. G. G. EXNER—Methods for Facilitating the Extraction of Teeth. |
| Mon. | 21 | 5.00 | DR. F. S. GORRILL—Arnott Demonstration.* |
| | | 5.00 | MR. F. T. MOORE—Hand Deformities : Reparative Surgery. |
| Tues. | 22 | | Last day for applications for Annual Examinerships. |
| | | 3.45 | PROF. W. E. GYE—Imperial Cancer Research Fund Lecture—The Propagation of Mouse Tumours by Means of Dried Tissue.* |
| | | 5.00 | MR. E. W. PEET—External Genitalia : Treatment of Congenital Deformities. |
| Wed. | 23 | 5.00 | DR. FRANK ADAIR—Moynihan Lecture—The Results of Surgery in the Treatment of Breast Cancer.* |
| | | 5.00 | MR. O. T. MANSFIELD—Hand Injuries (including burns) : Early Treatment. |
| Thur. | 24 | 5.00 | MR. K. BOWES—Arris and Gale Lecture—Infra-Red Photographic Studies of the Superficial Veins in the Female and their Clinical Application.* |
| Fri. | 25 | 5.00 | PROF. W. S. C. COPEMAN—Hunterian Lecture—Pathological Anatomy of Certain Forms of Lumbar Fibrositis and the role of Surgery in its Treatment.* |
| Mon. | 28 | | Demonstrations on Anatomy, Applied Physiology and Pathology begin. |
| | | 3.45 | MR. R. J. LAST—Arnott Demonstration.* |
| | | 5.00 | MR. D. BAND—Neurological Disorders of the Urinary Bladder. |
| Tues. | 29 | | Date of Council Election announced. |
| | | 10.00 | MR. A. D. MARSTON—History of Anæsthesia. |
| | | 11.15 | MR. A. D. MARSTON—History of Anæsthesia. |
| | | 5.00 | DR. B. L. S. MURTAGH—Avoidable Accidents. |
| | | 5.00 | PROF. A. FRANCESCHETTI—Cataract Associated with Lesions of the Skin.* |
| | | 6.15 | PROF. G. B. BIETTI—Protein and Animo-acid Deficiencies in Ophthalmology.* |
| Wed. | 30 | 10.00 | DR. H. G. EPSTEIN—Physics in Anæsthesia. |
| | | 11.15 | DR. H. G. EPSTEIN—Physics in Anæsthesia. |
| | | 5.00 | DR. G. EDWARDS—Pre-operative Medication. |
| | | 5.00 | DR. E. HARTMANN—Psychosomatic Symptoms in Ophthalmology.* |
| | | 6.15 | PROF. H. J. M. WEVE—Ophthalmic Manifestations of Besnier-Boeck's Disease.* |
| Thur. | 31 | 10.00 | DR. E. A. PASK—Respiratory Depression. |
| | | 11.15 | DR. E. A. PASK—Circulatory Depression and Shock. |
| | | 5.00 | DR. E. A. PASK—Circulatory Depression and Shock. |
| | | 5.00 | PROF. C. GRAY—Hunterian Lecture—Surgical Treatment of the Painful Hip Joint.* |

* Not part of courses.

# JOHN HUNTER THE OBSERVER

## THE HUNTERIAN ORATION—1949

Delivered at the Royal College of Surgeons of England

on

14th February, 1949

by

H. S. Souttar, C.B.E., F.R.C.S.

Senior Surgeon, The London Hospital

JOHN HUNTER WAS BORN in 1728 at Long Calderwood, a small estate in Lanarkshire, seven miles south of Glasgow, near the village of East Kilbride. He was the last of 10 children, seven of whom survived childhood. Of them, James, 14 years his senior, entered medicine and joined his brother William in London, only to end from phthisis a career of brilliant promise at the age of 29. William, 10 years the senior of John, was for five years a student at Glasgow and at first was destined for the ministry. At the age of 19, however, he joined Dr. William Cullen, who at the age of 27 had a busy practice at Hamilton, near Kilbride. They must both have been young men of enterprise for they arranged that in each winter one of them should study medicine in Edinburgh or Glasgow, while the other carried on the practice. In 1740 William Hunter attended Alexander Morris's lectures in Edinburgh, and in 1741, at the age of 23, he made up his mind to seek his fortunes in London. Cullen went to Glasgow where he became Professor of Medicine, but a few years later he moved to Edinburgh where he occupied successively the Chairs of Chemistry, Institutes of Medicine and the practice of Physic, and left a high reputation as a lecturer renowned for the clearness of his exposition.

William Hunter lived at first in London with Dr. William Smellie, another Lanarkshire man and a friend of William Cullen. Smellie had settled in London at the age of 42 after studying in Paris, and was just entering on a distinguished career in midwifery. He gave lessons in the art, using a real pelvis lined with leather for practical demonstration and he was one of the first to stress the importance of accurate measurements. William Hunter remained with him only a short time and became assistant to Dr. John Douglas and a surgeon's pupil at St. George's where he worked in the dissecting room. He visited Paris and it is evident that he made great progress in anatomy, for in 1748 he established his own dissecting room and advertised a course of lectures.

It was at this juncture that he was joined by his brother John, a raw redheaded Scottish boy of 20 who had so far given no signs of any ability,

William Hunter.

Dr. Cullen.

William Smellie.

who hated books and was evidently regarded as the black sheep of the family. To the amazement of everyone he settled down to his new life in the dissecting room as one born to it. He produced beautiful dissections and delighted his brother William who was rapidly making his

way in the field of midwifery and to whom this unexpected assistance must have seemed a gift from Heaven. At the same time he was a rough customer and a curious point in his favour was that he was a favourite with the resurrection men, upon whom the dissecting room was dependent for materials. It must have been a rough place, for all modern antiseptics and preservatives were unknown and dissection under such conditions was both unpleasant and dangerous and could only be carried on in the winter.

John Hunter (as a young man).

It is worth while pausing for a moment to consider these young men, Smellie, Cullen and the two Hunters, and the country from which they came. Glasgow itself was only a small town of 15,000 inhabitants, and the corner of Lanarkshire from which they all came must have been primitive in the last degree. Beyond this stretched the Highlands, a country without roads and in a state of barbarism beside which Afghanistan would seem civilised. Moreover, just before this, in 1745, the Highlanders had invaded England in a destroying horde, pillaging Glasgow itself and all the surrounding country on their way. It was such an environment, and not the quiet amenities of a university town, that threw up four of the greatest leaders in the history of medical science.

In the summer of '49, by his brother's influence, John Hunter, now 21, became a pupil at Chelsea Hospital of the great Cheselden, now nearing the end of his career. On his death in '51, Hunter became a surgeon's pupil at St. Bartholomew's Hospital, where Percival Pott was rising to fame. Finally, in '54, he returned as a pupil to St. George's Hospital where he was afterwards to serve as a surgeon for 25 years. In '56 he was appointed house surgeon, but after five months he gave it up in order to devote his time to anatomy. His interest now extended to the

anatomy and physiology of the whole animal world, and he worked from morning to night dissecting every animal he could find. Naturally his health gave way and in '60, after an attack of inflammation of the lungs, he obtained a commission as staff surgeon in the Army and saw three years of foreign service at Belleisle and in Portugal. His health recovered and in '63, at the age of 35, he returned to London and set up in practice as a surgeon in Golden Square.

W Cheselden.

Percival Pott.

While waiting for practice he again established a dissecting room and a school of anatomy, devoting the greater part of his time to preparing specimens and teaching students. In order that he might also study living animals and their functions he took a plot of land " two miles from London at a place called Earl's Court," and there he built a small house in which he could indeed live, but which was the centre of a most extraordinary zoo. Over the front door was the wide-open mouth of a crocodile. In the garden were many strange animals, including a couple of leopards and a pair of buffaloes which were occasionally put into harness and driven round London. A jackal, a zebra, an ostrich, a young bull and many smaller animals all lived together in perfect harmony.

It was scarcely an orthodox way to develop a surgical practice but he was acquiring a vast knowledge of comparative anatomy and his contributions to this new science were recognised in '67 by his election at 39 to the Royal Society. In the same year he ruptured his tendo Achillis, and this irrepressible man not only treated himself successfully on ultra-modern lines but performed a whole series of experiments on dogs to see how tendons united. During the next year he was elected a surgeon on the staff of St. George's Hospital and he now moved to his brother's old house at 42, Jermyn Street. It was a good house, suitable for a surgical practice

and into which he could take, as was the custom, a number of pupils in surgery. Among his pupils were several who rose to great distinction, and we find the names of Astley Cooper, Abernethy and Clive and Edward Jenner. It must have been a strange house, for already Hunter's one absorbing interest was in his collection. It grew until every available room in the house was filled with strange specimens, dry and bottled, covering the whole animal and vegetable kingdoms, whilst in the passage a giraffe appeared to be emerging from the floor below. How a surgical practice could be developed under such conditions is a mystery, but it gradually grew to large dimensions. Practice was, however, always a secondary consideration and every penny that could be spared went to the collection.

Astley Cooper

John Abernethy

Edward Jenner.

Of Hunter's daily life Ottley has given such a perfect description that I cannot do better than to quote it:

"He commenced his labours in the dissecting-room generally before six in the morning, and remained there until nine, when he breakfasted. After breakfast he saw patients at his own house until twelve, when he made it a point to set forth on his rounds, even though persons might be in waiting for the purpose of seeing him. . . . He dined at four, then the fashionable hour, and gave strict orders that dinner should be ready punctually whether he was at home or not. He was a very moderate eater, and set little value on the indulgence of the palate. During many of the latter years of his life, he drank no wine, and therefore seldom remained long at table after dinner, except when he had company. . . . After dinner he was accustomed to sleep for about an hour, and his evenings were spent either in preparing or delivering lectures, in dictating to an amanuensis the records of particular cases, of which he kept a regular entry, or in a similar manner committing to paper the substance of any work on which he chanced to be engaged. When employed in the latter way, Mr. Bell and he used to retire to the study, the former carrying with him from the museum such preparations as related to the subject on which Hunter was engaged; these were placed on the table before him, and at the other end sat Mr. Bell, writing from Hunter's dictation. The manuscript was then looked over, and the grammatical blunders, for Bell was an uneducated man, corrected by Hunter. At twelve, the family went to bed, and the butler, before retiring to rest, used to bring in a fresh argand lamp, by the light of which Hunter continued his labours until one or two in the morning, or even later in winter. Thus he left only about four hours for sleep, which, with the hour after dinner, was all the time that he devoted to the refreshment of his body. He had no home amusements, as cards, for the relaxation of his mind; the only indulgence of this kind he enjoyed consisted in an evening's ramble amongst the various denizens of earth and air which he had congregated at Earl's Court."

It was about this time that Hunter, at the age of 43, married Anne Home, the daughter of an Army doctor, and 29 years of age. She was a woman of great charm and considerable social distinction, the friend of Haydn, Madame d'Arblay and Mrs. Montague. She was something of a poetess and wrote the words for Haydn's "The Creation," and the song, "My mother bids me bind my hair," which in Haydn's setting is immortal. She must have had a difficult life, but she was devoted to Hunter and her appreciation of his work is shown in her touching epitaph inscribed on his memorial tablet in St. Martin-in-the-Fields. Only two years after their marriage, Hunter, at the age of 45, had his first attack of coronary thrombosis, and though he made a good recovery, the fear of angina shadowed the rest of his life. It only drove him to greater efforts to complete his work, but whilst his indomitable courage demands our unstinted

admiration, perhaps we owe a greater debt than we realise to Mrs. Hunter in the background.

Mrs. John Hunter.

In 1783, the lease of his house in Jermyn Street came to an end and he bought the lease of a large house on the east side of Leicester Square, and a house behind it in Castle Street, now Charing Cross Road. On the ground between the two he built a lecture room and a museum large enough to house his immense collection. In the Leicester Square house were his consulting rooms, whilst the Castle Street house was devoted to dissection and the preparation of specimens for the museum. This back entrance must have seen some strange sights, from the visits of resurrection men to the arrival from Earl's Court of the skeleton of Byrne, the Irish giant, which now stands beneath this very roof. A vast staff was employed and between the cost of this and the cost of the building Hunter expended on his collection more than £70,000. For two years this extraordinary man lived and worked in these extraordinary surroundings, a constant sufferer from attacks of angina and in the end, at the age of 65, its victim.

John Hunter was above all things an observer. He was devoured by a passionate desire to know how things were made and how they worked, and it was typical of the man that he realised that the only way to do this was to look and see for himself. Indeed, he summed up his whole outlook on life in his famous aphorism, "Do not think. Try. Be patient, be accurate." To us who grow from our cradles in a world of laboratories and research, it is difficult to realise how revolutionary such a proposal must have seemed to his contemporaries. For most of us all knowledge was contained in tradition and there was something almost indecent in attempts to dissect nature. To doubt the word of Aristotle was as perverse as to doubt the book of Genesis and was to uproot the foundations of all

John Hunter.

human knowledge. It is a mistake to suppose that the objections centred only on human dissections and the resurrection men, they went far deeper into resentment at any interference with what were regarded as established facts.

It was through this veil of prejudice and ignorance that John Hunter and his museum tore so completely, and it is this achievement which so amply earns our gratitude. The specimens in his collection are themselves of value but of greater moment is the lesson they teach us of the value of observation.

What precisely do we mean by observation and wherein lies its value? In a sense, every one of us is the product of observation for each of us is moulded by his reaction to environment. But scientific observation means something more than this. First of all it means enquiry, and enquiry means that we have asked a question. Something has happened that we do not quite understand and our curiosity is aroused. We try to produce the same event and to follow the train of circumstances which led to it. Then, and it is here that the genius of the observer appears, we modify the circumstances and see the effect upon the result. Nine times out of ten they all fit together into well-known categories, and though

our curiosity is satisfied, that is all. But just once in a while things do not quite fit together and then, if we are fortunate and have infinite patience and persistence, we may find a chink through which we may peer into one of nature's secrets. Let me give you some examples.

In 1785, Henry Cavendish, by passing an electric spark through common air, succeeded in making the oxygen and nitrogen substances, with which he was only vaguely acquainted, to combine together to form nitric acid. There was, however, a small residue, less than one per cent., of gas left which he surmised might be a gas of a different nature. A century had passed before Lord Raleigh astonished the world by the discovery of argon, the unknown residue which Cavendish isolated with his primitive apparatus. His observation was perfect, but no means then existed for its interpretation. Yet the observation itself was well worth while. The foundation of a building must be laid before the keystone is placed in the arch.

You are all familiar with the spectrum, that single octave in the vast range of ether waves which we call light and by which we see the world around us. To most of us it is just a series of brilliant colours, but to the physicist it consists of a vast number of narrow lines, each the product of a single length of wave, of a single pure tone in the harmony of light. These lines form definite groups and each group is the luminous signature of a burning element which, by this signature, can be identified even in a star a million million miles away. Thousands of these lines had been measured so that their position was known with extreme accuracy, but in spite of endless attempts no connection between these measurements could be discovered.

In 1885, a little Swiss schoolmaster in Basle named Balmer, felt an urge to research in physics and consulted Professor Hagenbach as to what he should do. The Professor, with a smile I imagine, suggested that he should find the relation between the measurements of the four principle lines of hydrogen.

The wave numbers of these lines, that is the number of waves in a centimetre, are:

15233·22 20564·79 23032·54 24373·06.

It did not seem a very hopeful problem, but to the amazement of everyone, Balmer returned in a few days with the answer. If you divide all these numbers by 109677·69, the result can be written in the simple form:

$$(1/4-1/9),\ (1/4-1/16),\ (1/4-1/25),\ (1/4-1/36).$$

Obviously, these are only the first four of a series and since his time, 50 more lines have been discovered, each taking its exact place in the series. Moreover, this curious number, 109677·69, is the magic key to the place

of every line in every spectrum. It is now known as Rydberg's Constant, and with it, Niels Bohr, the great Danish physicist, was able to unravel secrets of atomic structure which have revolutionised our whole conception of matter. But it was Balmer who found the key.

In 1900, Crookes devised a toy in which a minute speck of radium was placed in front of a tiny fluorescent screen. On looking through a lens you saw a shower of bright sparks. A young physicist named Rutherford from the backwoods of New Zealand, was intrigued by this and took the trouble to count the sparks under varying conditions. They proved the key to the secrets of radium and of atomic changes until then unknown, secrets which have already produced the atom bomb and which, if they do not destroy us, must certainly revolutionise our lives.

Some 25 years ago, Alexander Fleming found a spot of mould growing on one of his culture plates, and he noticed that none of the bacteria in culture grew near the mould. Overcoming his natural resentment at such an impertinent intrusion into his laboratory by a mere mould, he studied the intruder and found that it possessed the very remarkable power of preventing bacterial growth. He suspected that this might be due to some chemical substance secreted in the mould, but he had to wait 20 years for this substance to be isolated by Florey, and for the discovery of penicillin.

Now in each of these cases, the first observation was a simple matter, the genius of the observer lay in his appreciation that there was something here which he did not understand, some new fact outside his experience. He has found a door but he does not know where it may lead and he cannot open it until he has found the key. But the observation was the first step and without it the door would never have been found. And the initial observation is often so trivial that for most of us the event would have passed unnoticed and the observation would never have been made at all. Think of Cavendish with his primitive globes of gas; the little Swiss schoolmaster with his incomprehensible figures; Rutherford and a few sparks; Alexander Fleming and a spot of mould on a culture plate. Yet each was peering through a tiny window into a new world.

It is, however, only very rarely that the power to make observations and the ability to unravel their meaning are combined in the same individual, or indeed, that both can be accomplished in the same epoch. As we have just seen, years may elapse between the observation and the full appreciation of its meaning. It was in observation that Hunter was supreme and although within the limits of his time he often made acute deductions from his observations, his records are still worth our study as examples of what can be done with little more than unaided eyesight.

With such a great example before us, I feel that it will be worth while to devote a few moments to a consideration of " observation," to see in

what it consists, to study its uses and to examine how such power can be acquired and developed. In a sense, our whole lives are spent in observation, for when you come to examine it, you will find that our every action is a result of some stimulus and a reaction to environment. But this is not quite what we mean by conscious observation. Surrounded by a vast stream of events, of which fortunately we can only appreciate a minute fraction, we sometimes actively direct our attention to some detail which has aroused our interest. What is involved in such attention and under what conditions can it serve a purpose?

The mere fact that our attention has been attracted shows that something unusual has occurred, either in the external world or in its impact on our mentality. It is usually the latter, for nature is very conservative and rarely allows a variation, but in any case, the important fact is that to us the event was exceptional. I suppose that for countless aeons of time men watched the stars stream across the sky before one of these men noticed that one of the stars had moved from its place. But notice that that man himself must have watched the stars for years till their permanent relation was fixed in his mind and he was startled to find that one had changed its place. You can imagine that he kept the secret to himself and watched night after night to see if it were really true. And if he were a wise man, the more certain he became the more closely would he guard such a revolutionary discovery.

You see then that observation itself demands a background of conscious knowledge. Our first astronomer saw the stars as other men saw them, but with this difference, that up to the moment of his great discovery, he realised that they all kept their appointed stations, night after night and year after year. Without that background his observations would have been meaningless, with that background it was a discovery which marked an epoch. The first essential of all useful observation is then a background of established knowledge, that is to say, that imprinted on our memories is a pattern to which events around us conform, arousing perhaps our memories but without disturbing the pattern. In most of us the pattern becomes so fixed that variations pass unnoticed, and indeed since events are never exactly repeated, such assimilation of variation is essential if the pattern is to remain. But then one day we become conscious of some variation, perhaps because of its insistent repetition. Our interest is aroused and we stir ourselves to active observation.

Here men are divided into two great groups, the incurious and the curious. Of the causes of the divergence we know nothing, perhaps it is based on some endocrine or nutritional factor, but however that may be, we all recognise the man to whom discovery is the breath of life and the man to whom it is anathema. The latter is often a first-class teacher who not unnaturally fears the disturbance of his mental categories, the former may be a great researcher, but is often entirely unintelligible to

his pupils because he can never keep clearly before them the picture they require since his mind is too fluid. Just occasionally you find the rare mind with a clear picture but a burning curiosity which can inspire the pupils as well as the teacher.

I should say then that one essential factor in observation is curiosity. There are many kinds of curiosity from the mere desire to interfere with which we are all familiar, to the urge to satisfy some deep longing for comprehension, to resolve a discord in a final harmony. Whatever its true nature, it is undoubtedly an instinct essential for fruitful observation and one with which every teacher should seek to inspire his pupils. In John Hunter it was almost a mania and it was the steady driving force behind all his work.

A background of knowledge, curiosity, or the desire to extend it, are thus essential for fruitful observation, but something more is still required, the training of the power of observation itself. For the mere act of observation is not a simple act but a highly complex process in which many factors are involved and in the trained observer all these factors are subconsciously combined into a perfect unity, so perfect that its complex origin is concealed from the observer himself.

Each of us is given at birth eyes, ears and touch corpuscles in his fingers. Over these primary organs of sense we have little influence, we have fortunately little if any power of modifying their structure, and they do not appear to vary greatly from one individual to another. These different organs carry impressions to the nervous matter of the central nervous system and ultimately to the brain, the great central exchange for the correlation and synthesis of nervous impressions. As to how the brain works, we know very little, but two facts appear to be well established. After a very early age its cells never divide and therefore never multiply, but they have the power of forming connections with adjacent cells and of facilitating the passage of impulses by the reduction of the resistance at the synapse where they connect.

Each of us then is provided at birth with sense organs which he cannot modify, and a system of inter-communicating cables along which he can transmit messages, but to which he can make no addition. By constant repetition of one system of impulses he can, however, break down resistance at the appropriate synapses so that the message passes freely and without conscious effort. We can in fact develop a trained action or acquire a habit. We can modify or combine the impressions coming in through different channels so that far from colliding, they reinforce one another and resolve confusion into a single, clear, definite picture.

It is only by such training that the power of observation in any field can be acquired and a few examples will make this perfectly clear. The artist has trained his eye and his hand so that they work together in perfect

harmony and while he studies his subject you can see his hand already making the movements which will ultimately convey to paper through his pencil what his eye has grasped. Do you think that a violinist thinks where to put his fingers? He does not think about it at all for he knows that his ear and his fingers work together in perfect harmony and that they will give him all that he asks whether in brilliant cadenza or in subtle tone. And yet the artist and the musician do not surpass in the co-ordination they demand in the skill of the true clinical observer.

A physician is standing by a child's bedside, his fingers are on its wrist. He feels the dry, hot skin, he notes the racing pulse and estimates its power, its quality, its regularity. He sees the flushed face with its tinge of blue, he sees the nose expanding at each quick intake, he hears the hurried respiration and its characteristic grunt. And he knows that he is faced by an acute pneumonia with a certainty which nothing but direct clinical observation can afford. His long experience has gathered together a great number of separate impressions into one clear picture. He is a trained clinical observer and all his impressions are grouped together subconsciously into one observation which sweeps away irrelevant detail and grasps the one essential fact.

Perhaps I have chosen too simple an example, but the point I wish to stress is the value of trained observation and the great complexity of the factors which are involved in its achievement. I do not in the least degree undervalue the aids which science has placed at our disposal, chemical investigations, microscopical studies and X-rays for example, but all these are details to be assimilated by the observer and brought into the general picture, for without this co-ordination, they are all too likely to lead to errors.

Even elementary observation is the most difficult thing for a student to learn, and trained observation is only slowly acquired, but it is a power at which every student should aim from the first moment, and of which every teacher should enforce the value. For most of us visual impressions are the most important and these can be developed by attempts at drawing better and more rapidly than in any other way. However crude the drawing may be the mere attempt enforces observation and the shape of a bone, for example, can in a few minutes be fixed in the memory. The mere fact that one is rousing from slumber tracts in the brain so far unused, means an incalculable addition to one's powers. And if one can succeed in arousing by such means a latent curiosity, the trained observer is in sight.

This is the real problem of every teacher, how to teach his students to observe. Great variations in methods are possible and in no field of action is there greater scope for originality, but at least in a field so complex as that of medicine, certain broad lines must be followed.

First of all the student must be shown in detail all the essential elements of the completed picture which he should ultimately retain as a permanent pattern. Most of us are visualists and only what we have actually seen leaves a permanent impression on our memories. In continental clinics the lecture demonstration fills a more important role than it does in this country and I feel that we might make far more use of it than we do. I still remember a demonstration on Tuberculosis of the Spine given by the late Professor Hotz at Basle. It began with a series of fine pathological preparations showing every stage of the disease, with X-rays and photographs to show its clinical progress. A little man with an old healed angular curvature then came in, and he was followed by two bed cases, one of paraplegia and one of psoas abscess. In an hour we had been shown a complete picture of the disease so vivid that it still remains to me a living memory after 25 years. Such a demonstration involves resources in material and assistance which are rarely available, but can you question their incomparable value ?

Next the student must have access to specimens, to microscopic slides and to patients, so that he may study every detail of the picture at his leisure. In this College we are rapidly building up a pathological museum with this very object in view, where the student will find ready to his hand all the material for training his mind in exact observation which no book can supply. The patient himself must be studied in the hospital, but perhaps we may, in the very distant future, have even our own clinic for the more advanced study of disease.

With this experience behind him the ward demonstration will take on for the student an entirely new significance. Here the teacher can draw upon his own experiences and illustrate the points he desires to stress from the patients around him, while the student is introduced to the human side of observation as distinct from the purely scientific.

Finally, in the Out-Patient Department, the art is acquired of rapid recognition of main symptoms and their separation from a confused mass of unimportant detail. The student learns to recognise disease at sight, to become, in fact, the trained observer.

You will see then that the mind of the great observer is replete with pictures of definite entities, each a vivid and living reality based on an actual experience. It has been my good fortune to meet some of these great minds who leave so deep an impression on our own personality, and when I mention the names of Harold Barnard, Henry Head and Wilfred Trotter, many of you will be recalled to happy memories. With Barnard, every case was an adventure into the world of romance, every specimen a trophy from a voyage of discovery. To head a small area of increased sensation was an open sesame, a slight change in gait the key to deeply seated processes of vital import. The quiet glance of Trotter

could penetrate into the subtle instincts which to us unknown play so large a part in all our lives. Each was a great observer and each has left for us the golden harvest of what he saw and the gleaming inspiration of his example.

In the ancient world men looked within themselves for knowledge, and for them the world around had little interest. For us a vast field of Nature has been opened of which they knew nothing and it seems to be as limitless as the heavens. Whether we look down a microscope at a minute organism, or through a great telescope at a nebula a million years of light away, we realise that there is an infinity beyond. But infinitely small or infinitely distant it is there for us to see and it only awaits our observation. All around us are whole worlds for us to see, if we will only look, to hear if we will only listen.

> " What does it matter where or how we die
> So long as we have health to see it all
> The different ways that different things are done
> And men and women loving in this world ? "

Could a better epitaph be found for the great observer we honour to-day—John Hunter?

## THE RESTORATION AND DEVELOPMENT FUND

On February 14, the Anniversary of Hunter's birth, the President sent a reminder to those Fellows of the College who had not yet contributed to the Restoration Fund. Up to the date of going to press the amount received is over £1,300, including the following notable gifts: Two hundred guineas from Professor Brodie Hughes; one hundred guineas from W. D. Coltart, Solly M. Cohen, E. W. Peet, J. Clarke Mead, J. H. O'Donnell, Geoffrey E. Parker and Patrick Kiely of Cork; and fifty pounds from R. W. Knowlton and Ralph Marnham.

Many smaller donations have been received, and are deeply appreciated, for they provide evidence of the loyal attachment of the Fellows to their College. In addition, Sir Allen Daley, Medical Officer of Health for the County of London, sent an unsolicited gift in gratitude for the pleasure he had experienced in his visits to the College.

# JOHN HUNTER'S ACCOUNT OF A "MORTIFYD" APPENDIX CAECI

by

V. Zachary Cope, F.R.C.S.

Vice-President, Royal College of Surgeons of England

IN A MANUSCRIPT book in the Library of the Royal College of Surgeons is to be found the account of an autopsy in which is clearly described the condition of paralysis of the intestines associated with peritonitis due to a gangrenous appendix. This is the earliest record, in English, of such a case and for that reason and because John Hunter made the record, it would seem worthy of publication. Heister had noted a gangrenous appendix in 1711 and had described it in his "Observations," and Mestivier in 1759 and Lamotte in 1766 had published somewhat similar accounts of a diseased appendix, but no English or American account appeared before that of Parkinson in 1812.

Hunter's account is particularly noteworthy because the patient had been regarded as suffering from intestinal obstruction and Hunter, with his usual acumen, demonstrated that there was no true mechanical obstruction, and came to the reasonable and correct conclusion that there was a paralysis of the intestines.

The account is as follows:

*John Hunter. An Account of the Dessections of Morbid Bodys. MS. in various hands. R.C.S. Library* 49.*e.* 15.

*Case* 120 *is wholly written in Hunter's own hand.*

---

No. 120.

"I open'd Col. Delrumple who died of an inflammation in his Bowels joind with a Total stopage of his stools. He did not go to stool from the Tuesday to the Tuesday when he died. The Physic he took never passed thro him nor did the Clysters ever come away. In the time he had not starved himself, but had eat moderately. He had great pain in his belly and it was vastly [*distended* crossed out] tight.

On opening the abdomen I found that the Liver adher'd pretty firmly to the muscles there and also to the Diaph: I likewise found that it adhered to stomach by its left under surface; on the right to the Pylorus, beginning of transverse arch of colon etc. These adhesions were strong and of old standing. The Gall B: was about half full of Bile and its Ducts were clear. The Epiploon sound but not large, so as to cover the intestines. The small Intestines towards Ilium adhered to one another and to parts adjacent especially in the Pelvis, but this adhesion was of a soft glutinous nature wh. showd it to be

rescent and a good many red spots on the surface of Peritonaeum especialy on that surface that was in contact with the Peritonaeum of abdomen.

The apendix Caeci [altered by Hunter from *The Caecum* in each of the four places where it occurs] was vastly large and on squeesing the colon the air escaped thro the coats of the apendix Caeci. It adhered to parts it came in contact with and from it came about 3 ounces of a putrid matter which lay in the Pelvis. On feeling the apendix Caeci I found hard bodys in it, which proved to be a hard chalky Feces some as large as a Nut.

On examining the inside of the Intestines they seem'd sound excepting the apendix Caeci which was vastly inflam'd, ulcerated and in some places mortifyd. Near the termination of Ilium and Caecum they seem'd thicker in their coats than common, and appeard as if dropsied and on wounding them I could easily squees out a clear water.

There was a good deal of air in the stomach and the whole of the intestines, also a good deal of fluid which was mixt with Faeces in the colon. The Faeces in colon lay chiefly plasterd to the inside of its coats.

The whole small was clear.

The reason for his want of Stools must have arose from a Paralisis of the Intestine as no obstruction was observable even to the anus, and what strengthens this opinion is that he did not make water although there was water in the Bladder and still more strengthened by his loosing in a small degree the use of his limbs."

## REFERENCES

HEISTER (1755) *Medical, Chirurgical and Anatomical Cases and Observations.* English translation.

MESTIVIER (1759) *J. de Med. Chir. Pharmac.* **10**, 441.

LAMOTTE, DE JOUBERT (1766) *J. de Med. Chir. Pharmac.* **24**, 65.

## SAYINGS OF THE GREAT

" The method of experimental science is, beyond all shadow of doubt, the most effective implement for the advancement of knowledge ever invented by man."—*Trotter.*

# WILFRED TROTTER*

Presidential Address given at the meeting of the Surgical Section of The Royal Society of Medicine
on
3rd November, 1948
by

Julian Taylor, C.B.E., M.S., F.R.C.S.
Surgeon to University College Hospital

TO-DAY IS BY CHANCE the 76th anniversary of the birth of Wilfred Batten Lewis Trotter on November 3, 1872, somewhere on our side of the southern Welsh border and on November 25, 1939, he died. He suffered from spinal caries in youth so that he lay on his back until the age of 16. A year later he entered University College School, leaving in 1891 to study medicine at University College, London. He graduated as M.B. with distinction in medicine in 1896, later gaining a gold medal and scholarship in the B.S. examination, still later passing those for the higher degrees and diplomas. A frail childhood and lack of schooling did not harm him, for he was a highly cultivated person; indeed he attributed the remarkable familiarity with the Scriptures and their wording that betrayed itself in all his writing to the long days when he stayed in bed and read the Bible. If there was in fact anything lacking in his equipment for life, it was in other aspects that some would see defects, the filling of which might perhaps have made his life a more obviously happy one. For example he took little interest in foreign travel, foreign language, foreign countries or even foreigners; he had little appreciation of the unwritten arts; surprising as it may seem, the exquisite discrimination of his taste in letters, in manners, in social contacts, appeared to lack counterpart where music, pictures, furniture, objects of art and virtu were concerned. His artistic taste seemed to lie wholly in the perfection of natural form, thus a good drawing of a flower gave him something of the pleasure that he took in the trees of his Hampshire farm. Yet what schools in our country do bestow artistic tastes where they are not inbred? How many even foster them? What man ever fell short of English gentility because he lacked them? I think that the only real defect that may properly be attributed to an almost home-conducted education, was the absence from his later life of the close circle of friends that most of us recently looked forward to re-entering, when we should have done with the pestilent Nazis. There must have been quality in his education, and it must have come from his home surroundings, though I like to think that my own old school taught him his English Grammar.

I shall not trouble you with the domestic detail of his career and rise in our hospital, but in the Medical Faculty of University College in those

* By kind permission of The Royal Society of Medicine

days were luminous intellects, among which for him the most powerful influences were those of Rose Bradford and Victor Horsley. Medicine he thus learned in an atmosphere of intellectual clarity, but before Horsley's influence was felt, his first chief in surgery was Arthur Barker, an Irishman and of very different type. For Barker and his work he ever after expressed a respect far greater than his rarely shown antipathy to a personality so different from his own. Among Barker's merits were the open mind and eagerness which enabled him to pick out new and real technical advances, usually in Germany, and the dexterity and vigour with which he applied them. He was a great abdominal technician, but of surgical disease as Trotter came to know it, he had little apprehension, and, as one might expect with such a man if of forceful egotistical character, he was always known as The Master. The nickname affords a sidelight on the difference existing between the youthful attitude of the London student and that of his Continental brother. For even among our extremely intelligent, and to the point of cynicism, realistic friends, the French, even among them it is the custom for every surgical chief to be called le Maître, and mon Maître he remains to each of them ever after. Whereas we used the term as a familiar sobriquet that indicated that although with the perspicacity with which we endowed all medical students we saw his virtues, indeed we most of us asked to become his dressers, we hailed the claims of the Master's manner with reserve. It may be that the days of the great man and the habit of pomposity were already ended in London, to linger perhaps a little longer in a more northerly latitude.

But I should make it clear that in smiling at the claims of the grand manner we knew well that it was the Master who introduced into England the practice of asepsis, for from the beginning of the century onwards each dressing in Barker's wards had its own sterilised drum ready every morning. It was he, also, who brought from Courland Schleich's infiltration method of local analgesia, and from Biers in Berlin the practice of spinal. Such was Trotter's first surgical teacher, his very antithesis except in the possession of dextrous hands. Though Trotter never assigned to technical methods anything but a secondary importance, his fingers were skilful partly because he first learned his art from Barker, the man who brought to England so many things now the routine of surgery, but for whom it is probably true to say that technique was surgery. His other early teacher was Rose Bradford, whose brilliance as a physician and lecturer was in contrast also with the personality of Barker, devoid as the latter was of a grain of wit or humour. Already in the out-patients' department Bradford's teaching is said to have been the equal of his later lectures which were attended every morning by the whole school, and by the residents and registrars. Then came Horsley, and if Trotter owed to any the forming of his mind it was to these two. Horsley was again quite different from either of the others. He was a fanatical worker, a habit that Trotter certainly never contracted, and his contributions to

experimental medicine were as truly fundamental as was his work in surgery of the central nervous system. But perhaps if none but Trotter cast Trotter's mind, it was Horsley who formed the detail of his charming manners, for one had but to see the two together to be conscious of the unity of their reaction to externals. Attentive and receptive in conversation on any subject, but in fact contemptuous of confused thinking when revealed, they seemed almost identical. When Horsley had retired from our staff he would sometimes come to discuss cases with Trotter in our wards. Then the mask of manners would be lifted a fraction—but only to Trotter—for while he then became the dresser he had been, the House Surgeon was apparently Horsley's most respected colleague.

In the yet early days of which I am speaking Trotter began to impress and impose his personality on his fellows and his juniors, and from his student days until he joined our staff there flowed through our school a steady stream of men stamped with the technique of his thought, and also with as much of its essence as their respective intelligences permitted. As admirers usually do they imitated, and there are still small tricks of speech by which these men may be recognised to-day. Some have been highly successful, some not obviously so in the worldly sense, curiously few have been surgeons. All are characterised by a thoughtful attitude towards their work and lives and by charming manners. They are the first of his handiwork in human plastics, they are the results of his early psychological operations.

It was at this early time that he was formulating the philosophical conceptions that he enunciated in print a few years later and that at once brought his name into prominence in the thoughtful world. Nevertheless, in our hospital his surgery was already far in advance of his time, for there is a tradition, for which I can find no written confirmation, that he successfully removed a carcinoma of the cervical œsophagus while still surgical registrar. Yet there are few records of those days that name him even in our extremely active students' medical society, the minutes of whose meetings are a model. True to his later character he was sensitive and retiring to a degree and was also intolerant of the boredom that such meetings may entail.

Unluckily for Trotter there was at this time among his contemporaries the gifted and dashing young Rupert Bucknall who had qualities that Trotter probably then lacked more obviously than in later life. Bucknall was a good mixer, whose quick wits were more full-bodied and far more companionable than Trotter's, and it was as natural then, as it would be now, that he should be preferred for the next vacancy in our surgical staff. After this failure, which for financial reasons meant much to him, he was appointed to the staff of the East London Hospital for Children, where the effect of his presence seems to have been instantaneous, but by his personality and wits rather than by the volume of work that he accomplished. Nevertheless at that time he offered solutions to two difficult problems in the surgery of children. He designed and carried

out an operation for talipes equinovarus whose conception has been perpetuated in the Steindler operation for pes cavus to-day, and he also invented an operative treatment of congenital torticollis, modifications of which are now our standard treatment, for he excised the whole mass of contracted tissues achieving an immediate and permanent result that was in pleasant contrast with the fiddling and laborious tenotomies and plasters of the day. Characteristically, he did not put pen to paper.

At the same time he slipped into the anatomical department of University College, a scented haven for unemployed surgeons, rapidly gaining fame as a teacher formidable on account of his edged wit, accurate and unforgettable in his demonstrations. For Trotter a year or so of anatomy was time well spent. It was here that the beautiful anatomical practice of his surgery had its foundation, for he was able to synthesise in three dimensions his conceptions of the structure of the body. Few surgeons display so clear a knowledge of anatomy in the round as did Trotter in all his work, and by its virtue he could approach a structure from any suitable point on the surface with certainty and knowledge, so that set operations meant little to him. This clear and unambiguous vision of anatomical relations was the foundation of his early surgical success, for he began to apply it to the deeper parts of the neck, and thus it is probable that Thane's dissecting room gave him the conception of lateral pharyngotomy.

It is obvious that anatomical ignorance may engender either rash contempt or unenterprising timidity, and further that its existence may be cloaked by the use of set operations, which, however boldly they may lead to the depths, often take inadequate notice of the diseases for which they are employed. It was, for example, the discarding of the set operations on the tongue in favour of those designed to remove cancer with everywhere adequate margins that was Trotter's first gift to surgery, and though these operations were for years laid aside in favour of radium, they have now come back into our practice certainly where radium is for some reason either dangerous or unpromising. At the same time the subject of anatomy had the advantage that it was not full of perplexities and contradictions, an all-absorbing study, he had time to think.

At last he had a stroke of luck, for in 1906 Horsley resigned from our staff, I believe over a disagreement with our committee on the subject of specialisation, for as early as this he wished to practise neurological surgery only. It is interesting to note that a desire for the extension of the regional specialisation of surgery existed even then. It is also interesting to see how our overdue realisation of the unity of the body and the interdependence of its working parts is now breaking down the disruptive grouping that came with specialisation. At this present time, for example, the destruction of the sympathetic system in the treatment of high blood pressure is apparently the natural function of the vascular, the thoracic, the neurological and the urinary surgeon, indeed of anybody but the general surgeon, who, so far, seems to be holding aloof from the surprising

tendency of the day to operate more and more for less and less, if I may paraphrase a familiar cliché.

On Horsley's retirement Trotter was appointed Assistant Surgeon to University College Hospital. His practice was negligible, his resources intangible, but he had leisure, and two years later the philosophical world was startled by the appearance of two papers in the *Sociological Review* entitled "The Instincts of the Herd in Man and Animals." Together they are some 60 pages of large octavo, and though their matter and style are such that one must make continual back reference to the long opening, they show clearly the accuracy of his thinking habits, the certainty of his deductions, the clarity of his expression, the nicety of his language. They were, in fact, new thought precisely expressed, though their pages do not presage the simplicity and cadence of his mature style. If "The Instincts of the Herd in Man and Animals" are his first known fruits of leisure, perhaps also we may attribute the conceptions of living disease and recovery that later characterised his work and teaching as originating in the period passed in contemplation of the dead body, for if he could visualise the bodily structures in three-dimensional relation, his mind could see them in function.

Once a member of our staff, his personal characters rather than the yet unproved importance of his surgery were the focus of attention. His reputation at that time was reproduced in a song by our greatly beloved and now lamented E. W. Twining, " Comes at ten instead of nine, gigantic growths to undermine." This was not an exaggeration and the missing hour, or it might be two, had been spent, I believe, not in a press of work, but meditatively and happily in bed. From early times, for many years, his outrageously well-aimed and piercing witticisms delivered seemingly carelessly by frontal, flank, or rear attack, were the salt of the place. He was not the first to handle such conversational weapons in Gower Street, indeed, he followed a tradition, but efficiency and accuracy and economy of effort distinguished his play with them. The passage of years never discarded them but they ceased to alienate their victims as their use became rarer and an æsthetic rather than a destructive pleasure. For in later years if a slim rapier seemed to threaten a vulnerable part, though touched, this was never penetrated. There was always wit in his formal lectures, in his bedside teaching, in his choice of words for every day, and it had a quality once described as roguish by an epicure* of many things including humour. The fastidious art of his writing and of his ordinary speech was faultless, and its quality of restrained statement is known to the world. To commend it, however piously, is an unnecessary intrusion.

I have tried to present to you something of the man, and must now pass on to his surgical work. In 30 years it ranged over many fields, throughout which period he continued to perform the functions of a

* The late Mr. Warren Low

general surgeon both in hospital and in private practice. He liked variety, but not excess. For him an imposing programme of operations had no attraction, nor was he ever of those who value their services to mankind by the superhuman length of their lists. The short catalogue of his publications is an index of his varied interests, which, ranging over the whole body, had one character in common. They centred on the unsatisfactory, the formidable, the things that daunted others to inadequacy or inaction. Indeed, throughout his whole career it was difficulty that fixed his attention to a problem, so that to the day of his retirement an unusually formidable surgical case of whatever kind was like gunfire to a war horse.

The first common disease that attracted him was cancer of the tongue. Forty years ago there were available inadequate intraoral procedures; there was Whitehead's resection of half the tongue, and there were dreadful mutilations like Kocher's removal of the whole tongue through the neck. So soon as he turned his mind to the matter he saw that to remove an organ rather than a disease, especially for a disease that lacked respect for the boundaries of descriptive anatomy was at once an inadequate and a too extensive therapy. Never once did he perform such an operation. Among his earliest case-sheets, dated December, 1906, is a diagram in his hand of the removal of a cancer of the lateral border of the tongue with a half inch margin, which crossed the middle line widely but preserved the tip, so that the function of speech would be little affected. A bilateral gland dissection was done. The patient returned in 1910 with a new growth that was the consequence of leukoplakia as the first had been, and this also was removed. Soon he had the situations of growths in the tongue arranged in his mind with suitable approaches. There were those to be dealt with through the unenlarged mouth, those for which it was necessary to split the cheek for access, and those for which a division of the jaw, either median or lateral was necessary. There were ingenious removals of the inner table of the mandible where growths were adherent. His last contribution was the splitting of the fore part of the tongue itself to approach the vallecula and epiglottis. This final operation was evolved after designing and carrying out a neat little procedure by which a growth of the frenun linguæ may be removed in one piece with the submaxillary lymph glands of both sides, if necessary with a flake of the jaw bone at the symphysis. Not only had he soon arranged the cancers of the tongue as regards operative access, but he had also graded them in terms of the kind of malignancy to be expected in the different clinical types. In the matter of lymph glands at first he used to carry out the extensive clearances named elsewhere block dissections, but he decided early that in the case of the tongue its removal with lymph glands in one piece, after the method of Kocher, was unsatisfactory. He was troubled by the problem of the region intervening between the mouth and neck operations. The evil of the gland dissection was that while it dealt with embolic growth, it left a possibly infiltrated

area in the floor of the mouth. So his final solution of the problem was that where possible the tongue growth and the submaxillary glands should be removed in one piece, that is to say the probably infiltrated area, and that on another occasion the rest of the neck could be cleared, this taking care of the embolic. His observations had led him to believe that in many growths of the anterior two-thirds of the tongue, the submaxillary fascia formed a barrier to the extension of the infiltrative process. Posteriorly, however, the barrier did not exist. In the mouth he habitually achieved healing by first intention, with the exception of slight infections around wire sutures in divided jaws. He relied on the closure of dead spaces, and the application of large muscular surfaces one to another. With limited gland dissections of the neck carried out in one piece with growths of the mouth the same result could be attained. He saw that the body developed local special immunities, especially in normally infected regions like the mouth. The healing of both primary operations on the pharynx, and of their later secondary closures, were compelling evidence of the truth of the conception.

At this time also he was attacking the nasopharyngeal growths whose clinical picture he described with Dr. Wilfred Harris, naming them endotheliomas, by means of osteoplastic temporary resection of the upper jaw, but he soon found that they could not be extirpated thus and abandoned them as inoperable, so that these operations disappear from his case books after 1911.

I will here interrupt the story of his cancer work for another early interest, the surgery of Graves disease. In 1907 this first year he operated upon three cases without a death; in 1908 there were 10 cases, with one death from empyema a fortnight after operation, in 1909 18 with two deaths. But this was not original work, for his senior colleagues Barker and Pollard were then doing similar operations, and Horsley had done many certainly since 1902. In that year he removed one lobe for exophthalmic goitre, and the other in 1904 for recurrence of symptoms. In 1906 he transplanted a piece of thyroid into the lady's abdominal wall to combat the resulting myxœdema. All these operations for Graves disease were carried out under chloroform anæsthetics. Trotter's method for years was hemithyroidectomy followed after a pause of some months by a less extensive operation on the other side. The results so obtained were in no way inferior to those that follow the modern subtotal thyroidectomy; indeed I have the impression that they were better and more certain but cannot substantiate it. It is interesting in the records of some of these early operations to see notes in Thomas Lewis's handwriting regarding cardiac irregularities, though auricular fibrillation is not mentioned. It is evident that at this time, long before the introduction of iodine therapy, these operations were not the death-dealing procedures that many have imagined, nor did they deserve the condemnation with candle and book that they received from physicians about the year 1910.

To return to malignant disease about the mouth, the growths in the posterior part of the tongue that often involved the pillars and the jaw led him to the pharynx, which at first he approached through a divided lower jaw. In 1909, however, he removed a growth of the arytenœpiglottic fold resecting the ala of the thyroid cartilage on the way for access, and I believe this must have been his first lateral pharyngotomy.

The story of the recognition of the varieties of tongue carcinoma was repeated for the pharynx and he soon established the truly remarkable sex distribution of the various pharyngeal growths. I feel sure that in these observations he was helped by a number of laryngologists, notably Herbert Tilley and E. B. Waggett. In his Hunterian lectures in 1913 this work was presented and it is remarkable in these days of percentages and logarithms that the very few cases that Trotter had at his disposal, an inadequate figure by Continental standards, afforded him all the observations necessary. He stated for example that post-cricoid carcinoma, meaning of course the growth that begins in this region, not primary œsophageal cancer that has spread upwards, occurs exclusively in women. The absence of operative exposure when radiotherapy is used, has since resulted in a lapse into confusion, but I wonder if anyone has ever seen a true post-cricoid growth in a man. In spite of small numbers this paper has stood the test of time, and the obvious comment is that accurate observation followed by accurate thought is a straighter route of progress and less encumbered, than the collection of figures, especially of other peoples', the so-called statistical method.

His work in the pharynx had begun with the proposition that there was neither reason nor virtue in the customary removal of the larynx for cancer of the pharynx, a truth obvious 40 years ago to Trotter alone, but self-evident to us since he pointed it out.

Next, he turned his attention to the larynx, and carried out radical removals of growths by partial laryngectomy with preservation of the voice. In all these pharyngeal and laryngeal operations an important part was the prevention of serious infection of the neck and of spread of infection to the mediastinum. The latter aim was accomplished by suture of the sternomastoid to the longus colli. When he had learned to reduce or abolish infection of the neck after resections of growths of the pharynx, secondary closures, reconstructions of the pharynx and larynx from the skin of the neck became precise operations with little resulting scarring or stricture, a complication that was troublesome in some of the early cases. He came to rely on careful exposure with no unnecessary opening of fascial places and on the local immunity of the tissues to their own particular bacterial life. The only chemotherapy that he used were the protection of the neck with perchloride packs while the pharynx was open, and sometimes the filling of the open neck with boric acid powder, usually with an apology to the supposed moderns that were present. Once the pharynx could be opened without fear, the problem of the pharyngeal pouch was solved and I doubt if he ever did anything but

the removal in one stage, that is now the established procedure and that has displaced all others. In the years before the 1914 war, with H. Morriston Davies he placed renal hypernephroma in its present clearcut position as a malignant entity with individual habits, his contribution being untouched by any later disputes as to its correct naming. With Charles Bolton a little later he described the nature, symptomatology and operative treatment of gastrojejunocolic fistula, from observation of, I think, four cases. These last two were formidable diseases encountered by a general surgeon in his ordinary work, but for originality of conception it is probable that his work on the nervous system was the equal of that in malignant disease.

His first entry into this field was the section by himself and H. Morriston Davies of certain of their own cutaneous nerves and the observation of the effects, and of the quality of returning sensation. These experiments failed to confirm certain current views regarding epicritic and protopathic sensation, and like the rest of his work their conclusions have stood the test of time. His next contribution was the publication of a clear account elaborated from the study of a very few patients of the, at that time, little understood condition of chronic subdural hæmatoma, a description that established its relation to injury and that again has needed neither alteration nor addition. In these early days he was known to us as our neurological surgeon but to only a limited circle outside our hospital. When, however, there appeared in Choyce's System of Surgery an article on the surgery of the brain, in this subject he also assumed the position of a leader for Horsley was now dead having succumbed to malignant malaria in Mesopotamia during the first world war. Included in this article was a section on injuries discussing their probable morbid anatomy and physiology and the nature of the associated disorders. It is largely original, and records observation and thought that might have been embodied in years of contributions to journals by lesser men, and again his conclusions were reached without a single reference to collected figures. Not quite all of this is firmly established for all efforts to demonstrate by experiment his physical explanation of the phenomena of concussion, have failed to prove that there is in fact a sudden enormous increase in intracranial pressure from temporary deformation of the skull, nor does his conception of generalized contusion of the brain as the cause of post-concussional symptoms find complete acceptance at the present time. Insistence on an organic rather than a psychological origin for such troubles is the lesson he taught, though his explanation of their pathogenesis may need amplification or modification.

So far I have tried to recall a little of the making of a famous surgeon. Now I wish to attempt to tell you something of what he meant to us in our hospital. Among the many things that he taught us by example was the approach to patients. In the out-patient department which it was his pleasure to attend to the end of his time it was his habit to listen attentively to the longest and most rambling story alike from the neurote and the husky

old slum lady, with the same courtesy that he probably paid to duchesses, a group of patients whom, unlike some eminent doctors, he never was heard to mention. He never interrupted, but gradually led by agreement and sympathetic inquiry to things that might be important for the matter in hand. This charming delicacy of approach to the mind and personality was then equalled by the extreme gentleness of his physical examination, for I think I never saw him hurt a patient. One of his stock complaints about doctors was their too common neglect to observe the elementary principle that to secure co-operation patients must not be unnecessarily hurt and never unwarned, and for Trotter the interpretation of unnecessary was strict. He would instance the well-known consequence of this kind of failure, in the response of the patient who, asked " am I hurting you " so frequently says " not yet doctor." Yet when a patient had left it was clear that the sympathetic approach that in fact transformed his patients of whatever class, education or intelligence, into his slaves, disciples and worshippers, so that they listened to him as to none other, was not the uncritical sympathy of the missionary. For his subsequent dissection of the story and often of the patient's mind, was apt to be amusingly destructive, sometimes by no means strait-laced, and if the patient had been a thought superior, perhaps as contemptuous as his handling had been courteous. Having been his dresser and Barker's, I had the luck to be his first house-surgeon when he was appointed to our senior staff in 1914, in which year, for the first time, but not for the last, I learned to dislike the Germans, whose pugnacity cut short by some months a time when I seemed to be on the pinnacle of existence. His teaching methods with me and my dressers were really an amplification of his approach to patients, but we were honoured in that he used to permit himself the free exercise of his lambent wit, the effortless placing of his sharpest darts straight into our self-consciousness. The resulting thickening of our skins has stood us in good stead ever since. From his point of view our minds were as clogged and muddy as the patients', but it was his task to teach us.

Always concerned with principles he would patiently talk to us and try to kindle in us some spark of cerebration on the matter in hand. A witty or a depressed comment would show that he had failed as he had indeed expected, but he would patiently try again and again, until it was obvious, even to our thickheaded selves, that we had been led by observation, thought, and simple reasoning, to some clearly useful deduction, commonly one with immediate and practical application. A thoughtful consideration followed by a practical conclusion was his usual method and never the one without the other where a patient's welfare was concerned. Once when he presided at a dinner I pointed to this character in his approach to clinical problems and was rewarded next day when Trotter took me by the arm to thank me for what he said was the greatest compliment of his life. He was tired of being fêted as a philosopher, no one else had ever called him practical. He said that he

was glad that he had at least impressed somebody with the idea that the brain is of some use. The intimate relation between observation and deduction that characterised all his work was seen in his knowledge of patients' states during operations. Warnings from the anæsthetist were superfluous, in fact such cautions tended to pass in the reverse direction, and to be extremely amusing. He would never have blood pressure recordings during extensive procedures on the brain for, exposed, it was a manometer to him. Indeed all tissues revealed their states to his apparently casual glance. The following incident illustrates his capacity to interpret quickly what he saw. Many years ago, at his request, a house-surgeon was removing a child's tonsils. Trotter walked in, his eyes as usual on the ground. They saw no blood on the floor, and lifting confirmed the conclusion that the child was not breathing. Attention to the tongue and one or two compressions of the chest restored both respiration and bleeding. It was a matter of seconds, and danger over he left the room, his eyes again on the ground, softly murmuring "very nearly dead."

Why was it that in our, at that time critical and candid, school he came to receive a respect and adulation that in a more normally conventional tribe would have been plain hero worship? It was because the clarity of his thought led infallibly to perfection in his work; because the skill that he employed in its execution was the match of its thoughtful inception; and because his bearing towards his patients was in its sensitive courtesy the complement of thought and dexterity. Probably no school could at that time have been better suited to the development of his qualities, for the habitual pathological truth of his estimate of disease and of the real effect of therapeutics was not of his introduction. But he specially and continually taught us by word and example that since our work is conducted on people and not on their bodies, an intellectual conception of disease as opposed to the rule of thumb, *implies* the exhibition of sensitive and gentle sympathy. The peculiar quality of his approach to the sick was a gentleness that had nothing of the feminine, nor roots in affection for his fellows. It was gentle because his brain made it so and thus it was highly efficient in attaining the therapeutic results for which it had been designed. It was enough that the working of his brain wrought the expected effect; that it made of every patient a worshipper, of every doctor a lifelong adherent, and of every junior an envious and despairing disciple, was a secondary and often fatiguing issue.

His operative methods matched the perfection of the rest. Simplicity of equipment, exclusion of the unnecessary, deliberation, manual ambidexterity, and the gentlest of touches made up a style in which there was no element of display. He understood that surgery is not carpentry and that once the surgeon has effected some simple form of temporary repair or readjustment, the real joinery is done by the body. He thus disliked any concentration on technique and the tendency of so many surgeons of his time to confuse it with surgery. Technique was for him the capacity needed by every surgeon to do his work with minimum trauma and

minimum pain to the sufferer. It was the necessary equipment of all surgeons and needed no more than passing comment, for why should one teach one's colleagues the elements of their job? So simple, clean, tidy and efficient, were his methods that there were those that their perfection escaped, from whom their art was concealed. They missed the burnished ornaments of the altar, the ritual, the white assembled acolytes. A very famous surgeon* once made this mistake when, in our theatre, he told Trotter that his brains were outstanding but that he had no technique. At Trotter's urbane reply that he valued so great a compliment from such a source the great man purred, but a little doubtfully, I think just conscious that there was a hint of obliquity in the exchange of compliments, but fortunately having no inkling that he was in fact being told that his surgery must be still in the elementary stage of carpentry. No one, it was said of Lord Melbourne, ever happened to have coats that fitted better.** No one ever happened to operate so simply and effortlessly as Trotter. It was great art concealing a greater.

Returning from the first war I found that Trotter had now assumed his place. The five shattering years had dragged through their destructive if usually boring course, but during them an unusually intelligent member of the Government had had the sense to ask Trotter to republish his essay on the instincts of the herd, as the basis of a book that should explain the Germans to the world. All of us have read it and all of us now know that his prophecy has been twice fulfilled, how the herd of wolves when it at last feels its enemy to be the stronger, will not become closer knit, but will rather lose its cohesion, disperse into individuals, and run.

One cannot be thought guilty of political prejudice if one senses the lack of similar brains behind our leaders to-day.

Trotter was now the acknowledged brain of surgery in Britain. He was sought in difficulties of every kind, and in the mouth, the pharynx, the thyroid, and the central nervous system, he was supreme. London seemed to be full of doctors who wanted no other opinion, he skimmed the cream of practice. He had the Royal Appointment and justified it by his help during the illness of His Majesty King George V in 1928. But he already preferred the seclusion of his Hampshire farmhouse to the lure of the enormous practice that was his for the assembly. He never was attracted by the lure of numbers nor by what it is now fashionable to call the team, for his work in private and hospital practice was completely personal in its character, so that even post-operative dressings were his own care, even if they shortened his week end escape.

After some years more the later period of his life was entered, for just as the life of Louis Quatorze, the Sun King whose personality and mind were utterly unlike Trotter's, was divided by serious illness into two periods, the brilliant and the quiet, so was Trotter's, by a malady

*Lord Moynihan

** The Young Lord Melbourne by David Cecil

that left a permanent frailty permitting neither exertion nor long hours of work.

It chanced that about this time the development of radiotherapy in the treatment of cancer attracted large numbers of sufferers to the apparent miracle, and that among these were included the victims of cancer of the upper respiratory passages. Thus his need for rest coincided with a rapid reduction in the volume of his work. None was more anxious than he for the success of the new agent, for if such wonders could be accomplished for the inoperable cancers surely the operable ones might be similarly benefited.

He smilingly said that his operations had not had a chance. His patients would certainly not have agreed with him then, nor do I think that now, twenty years later, would any surgeon. For dissections of the neck are the rule again, operations for cancer of the tongue and mouth are frequently performed, and these operations are those of Trotter such as I have shortly described them.

Would anyone at the present time confidently assert that to a woman suffering from post-cricoid carcinoma, radiotherapy has anything better to offer in substitution for lateral pharyngotomy?

The later stage of his life had, however, undoubtedly set in and in our hospital it was hard to see his failing physique. Some change had to be made and he might have done what others have in like misfortune, he might have left hospital work to his deputies and continued private practice. Not Trotter, for on a certain April day he gave up private practice but continued his hospital work without interruption. Shortly afterwards Mr. Choyce, our whole-time professor of surgery was unluckily forced to resign, also from failing health, and we persuaded Trotter to succeed him for his few remaining years of office. For about three years he was our professor and this was indeed fortunate for a group of assistants. For at once the Surgical Unit became a surgical nursery. However brilliant a young man may be and however responsive, to teach him even the niceties of the cure of hernia, is neither recreation nor attractive duty, yet Trotter spent many such hours in the theatre during his last few years, evidence that, intolerant as he was of boredom, he could subdue his inclinations in favour of that which he had laid down for himself as the professorial function. To some it may seem curious that this great and gifted surgeon famous for his scepticism, for his devastating criticism, and for his personal remoteness, should dedicate his last remaining years to his juniors, but the reason is not far to seek. If his own brain had been the source of surgical progress he must do something more than teach others what he himself had learned. He must complete his task by educating the brains of others, polishing their processes of thought so that they in turn might be imbued by his lifelong conviction that the brain is of some use. And he liked young people.

Honours came to him. The Council of the Royal College of Surgeons for the Presidency of which he had neither the health nor inclination.

The Royal Society in 1931. Honorary Surgeon then Serjeant Surgeon to His Majesty the King. Presidency of the Association of Surgeons, the Gold Medal of this society in 1938 and many honorary degrees. It was no secret that the Royal Society and the Royal College paid special heed to his counsels. Unfortunately about this time his health began seriously to fail and for the rest of his life he preferred to perform only those public functions that he knew were the duty inherent in his exceptional gifts. In 1932 he delivered at the Royal College of Surgeons the Hunterian Oration taking as his subject "The Commemoration of Great Men." In this remarkable lecture he chose the theme that it would be better to help great men during their lives than to commemorate their deaths. It was in the best style of his maturity, its penetrating criticisms, its crystal wit, the polished art of its wording affording his hearers a momentary entry into the working of his mind, a flashlight on the originality and range of his thought. His choice of language on all such occasions, as in private conversation, was appropriate to the keenness of the matter, and often modelled on the scriptures but lacking their repetitive habit, its biblical simplicity gave him a personal and epicurean satisfaction.

The Commemoration of Great Men is one of ten addresses that have been bound together in a memorial volume by the Trotter Memorial Fund of University College Hospital. They were delivered as opportunity offered to greatly differing audiences, for he was sure of packed houses, and afterwards of readers everywhere. All were prepared with the greatest care, with long consideration and repeated rewriting, as much, I think, for his own pleasure as for that of his hearers. I doubt if any student of Trotter's writings could find any real evidence of intellectual growth during his life, though I naturally also doubt my capacity to assess such a possibility. But his style shows considerable change within the limits of a fastidious taste. When I first knew him he often quoted George Meredith, evidently sharing this author's literary ideals, which dictated that every word must be selected for exact meaning and emphasis, and must then be set into place where it fitted like a part of a machine. The machine, however, could not be called a fast- or a smooth-running one, and a result of the method is that few sentences can be understood and their meanings completely assessed at the first reading. He also seemed then to be fond of Robert Louis Stevenson, savouring happily his adjectives, his similes, his careful though apparently light hearted construction. Later he came to favour a simpler style and I venture to quote and to compare two extracts from Trotter conveying almost the same idea. The first is an early one from "The Instincts of the Herd": "Man's resistiveness to certain suggestions, and especially to experience, as is seen so well in his attitude to the new, becomes therefore but another evidence of his suggestibility, since the new has always to encounter the opposition of herd tradition." Every word has its special importance but the whole needs reflection before the full meaning is grasped.

The second is from the last paragraph of his final address, that to the students of St. Mary's Hospital: "We like to suppose ourselves easily receptive of the new, and that by virtue of a natural mechanism. Unfortunately, this is the exact opposite of the truth. The mind likes a strange idea as little as the body likes a strange protein, and resists it with a similar energy." The sentences are short and vigorous, their meaning at once clear. Yet the style of these later papers is the development of the earlier, a polished prose almost concealing the art of its composition, and felicitous in choice and use of words in their exact meanings. The words were clearly those of a literary æsthete of pure and primitively simple taste. He never fell into the common error of making the words more important than the matter. At the same time there bubbles throughout them a peculiarly impish and attractive humour that is reminiscent of Shaw at his best and least provocative, though Trotter's is the sharper and is wielded with greater delicacy of touch. A hundred years before the first of these quoted sentences was written, Lord Melbourne in his youth made the observation that man could learn only by experience. A hundred years before the second, he said "Nobody ever learns anything by experience, everybody does the same thing over and over again." Here is something that Trotter saw plainly when quite young, but that took a great realist a lifetime's disillusion to learn. I cannot leave the subject of Trotter's writings without a reference to the wide extent of his reading in every sort of subject. Although the greater part of his contribution to knowledge came from his own brain, he was not in any sense indifferent to the workings of those of others, rather he was fascinated by them.

It needs no more than your presence to-night to confirm my impression that Trotter's memory is a living influence, after nine years he is not relegated to the dated pigeon-hole that is the niche of most eminent surgeons. His vital persistence is due in no small degree to the contents of this slim volume*, which, I was recently told by one of his colleagues on the Royal Society, are quoted more and more widely as the years pass. No one in our time was more justly appraised during his life, and it seems likely that to perpetuate his memory no orations are necessary. He was not attracted to formal solemnities of the kind, indeed his own point of view regarding them may be thought to be expressed a little crudely in an epitaph from the eighteenth century deciphered in a country church-yard by Sir Leslie Stephen:

> "Traveller pass on nor waste your useless time
> In lying eulogies or far worse rhyme.
> For what I am this mound of earth assures,
> And what I was is no affair of yours."

---

* The Collected Papers of Wilfred Trotter, F.R.S.

Wilfred Trotter

There are few good portraits of Trotter, they are mostly posthumous, clayey, and without life. This that I show you is a little different from the others for it is a small silver relief by Mr. Paget. It is with an uncomfortable sense of impiety that I look at this photograph because I remember an occasion when at a meeting of the council of the Association of Surgeons, Trotter disposed of a suggested demonstration by saying simply " Slides are substitutes for ideas.". This medal is the best portrait of Trotter that I know, and was struck at the wish of the Trotter Memorial Fund. It is the first surgical award that a new student may gain in our hospital, it is given for clinical surgery. We are sure that this is the commemoration that he would have chosen for himself, we hope it is not a substitute for ideas, we try to make it a reward for them.

## "OBSERVABLES" AT THE ROYAL COLLEGE OF SURGEONS

### 15. PICTURES BY GEORGE STUBBS, R.A.

GEORGE STUBBS was born in Liverpool in 1724. He died in 1806. He was, therefore, a contemporary of John Hunter. He was famous as anatomist as well as artist. He studied human anatomy, and gave lectures on the subject to hospital students. He illustrated Dr. John Burton's "Essay towards a complete new System of Midwifery," which was published in 1751. There is a copy of this book in the College Library.

Stubbs came to London in 1756 with a considerable reputation as a painter, especially as an animal painter. He charged 100 guineas for a portrait of a horse, to which animal he devoted years of study. In 1758 he took a farmhouse near Barton, in Lincolnshire, where he worked assiduously on his great book, "The Anatomy of the Horse." He dissected, and made complete and careful drawings of his preparations. He spent six to seven years over the illustrations, and the book was published in 1766. A copy of the book, which is still an acknowledged authority on the subject, is in the College Library, and the original drawings are in the library of the Royal Academy to which they were presented by Thomas Landseer.

In 1803, near the end of his life, Stubbs embarked on another anatomical work—"A Comparative Anatomical Exposition of the Structure of the Human Body with that of a Tiger and a common Fowl." Only three of the six intended parts were completed, and they also are to be found in the College Library. Stubbs's desire as an artist was "to look into nature for himself, and consult and copy her only." He was the first painter who thoroughly mastered the anatomy of animals. He was at his greatest as a painter of animals, and greatest of all as a realistic painter of horses. He also painted some heroic compositions, such as "Phæton"; "Horse affrighted by a Lion"; and "Hercules and Achelous." "A Lion seizing a Horse" often recurred among his paintings, based on an incident which was impressed vividly on his mind by having seen, whilst in Africa, a lion stalk and seize a white Barbary horse. His rustic pictures, like "The Farmer's Wife and the Raven"; "Labourers"; "Haymakers"; and "Reapers," were also among his popular works.

It would be natural for Hunter and Stubbs to come together, and it is not surprising to find among the pictures in the Hunterian Collection three by this master of anatomy, and master-painter of animals. All three are rather out of the ordinary, which, again, is no matter for surprise, but it makes the pictures of special interest because they are unique examples of Stubbs's work. One is of a Yak which was brought to England by Warren Hastings. Another is of an Indian Rhinoceros. The third is of a Baboon and Macaque (albino) which were dissected by Hunter.

W-J.

Painting of a Yak by George Stubbs (*Hunterian*).

Painting of an Indian Rhinoceros by George Stubbs (*Hunterian*)

Painting of a Baboon and Macaque (albino) by George Stubbs (*Hunterian*)

The Hunterian Dinner.

# THE HUNTERIAN DINNER

THEIR ROYAL HIGHNESSES the Princess Royal and the Duke of Gloucester honoured the College by attending the Hunterian Dinner which was held in the Library of the College on Monday, February 14.

A loyal message in the following terms was sent to The King:

"The Council and Court of Examiners of the Royal College of Surgeons of England meeting at the College, with Trustees of the Hunterian Collection and Honorary Fellows, on the Anniversary of Hunter's birth, with their humble duty beg to offer their loyal and devoted greetings and their best wishes for Your Majesty's speedy recovery. They also wish to express their deep appreciation of Your Majesty's constant interest and encouragement as Visitor of the College.

"Among the guests are representatives of the Commonwealth and other countries which have made remarkable contributions towards the restoration of the College. It is hoped to submit plans for Your Majesty's approval at an early date."

To this message His Majesty was graciously pleased to send the following reply:

"I should be grateful if you would express to all assembled at the Hunterian Dinner my sincere thanks for their kind and loyal message together with my best wishes for the continued prosperity of the Royal College. I shall look forward to seeing the plans for the restoration of its buildings which its friends in this country and from overseas have so generously furthered."—GEORGE R.

The Princess Royal responded to the Second Loyal Toast and stated that her brother, the Duke of Gloucester, had said it was her turn to speak as he had spoken at the last Hunterian Dinner. Her Royal Highness said it was very appropriate that she should do so since it was the first occasion on which women had been present at this historic dinner.

His Excellency the High Commissioner for Australia, the Rt. Hon. J. A. Beasley, in proposing the toast of "The College," recalled that he had attended his first Hunterian Dinner in 1946, three days after his arrival in England. He had always remembered the friendly atmosphere which he had encountered. He was very impressed with the educational activities of the Royal College of Surgeons of England and they were very deeply appreciated by post-graduate students from Australia and other countries. Graduates often told him how grateful they were to find that they had an academic home at the College, and so did distinguished surgeons from his country who always found a warm welcome. Mr. Beasley paid tribute to the enormous success of the Arthur Sims Travelling Professorship and said that Sir Hugh Cairns' visit had borne rich fruit. It was gratifying to learn that the Primary Examination for the Fellowship of the Royal Australasian College of Surgeons was now accepted by this College. He understood this was the first exemption which had ever been granted. The exchange of visits at the highest level had not been provided for in the past, continued His Excellency, although there had been provision for the exchange of students and young graduates aspiring to specialist status. The exchange of visits by leading teachers and research workers would be of increasing benefit to all countries of the Commonwealth as time went on. The recent announcement of Lord Nuffield's gift of a College of Surgical Sciences incorporated in the Royal College of Surgeons had been warmly welcomed in Australia and throughout the English-speaking world. Mr. Beasley said that it would provide a wonderful experience for young graduates to be able to live in the College of Surgeons and meet the

leading teachers of this country, as well as distinguished visitors from other countries, in the intimacy of collegiate life instead of only making contact with them in the laboratories and classrooms. He went on to say that London was the most wonderful centre in the world for post-graduate medical education, and if all the medical institutions would work together they would, by their co-operative effort, attract the best of the graduate students from the English-speaking world. " To-day," Mr. Beasley continued, " there is a wave of propaganda, untruthfulness and lies, all over the world. It is difficult to understand how it has gathered momentum, but it cannot be ignored. It calls for the widest influence from your profession, which has the responsibility for carrying humanity down the road. All those with a capacity to think and lead should emphasise that human values transgress all others."

The President, Lord Webb-Johnson, responding to the toast of " The College," referred to the fact that it was an historic occasion and said : " It is the first time that ladies have attended the Hunterian Dinner, so that quite apart from the honour that the Princess Royal and the Duke of Gloucester have done us this evening, Her Royal Highness is making history. I am somewhat ashamed when I recall that Royal Ladies have attended the Hunterian Oration in the past but have not been offered dinner. It is 40 years ago to-day since Queen Mary, as Princess of Wales, attended Sir Henry Morris' Oration, and it is 22 years to-day since the Princess Royal attended Lord Moynihan's. This seems rather belated hospitality."

The President thanked Mr. Beasley for his tribute to the work of the College, especially in post-graduate education, and in maintaining contacts with other countries. He agreed with His Excellency that the Arthur Sims Travelling Professorship had proved of enormous value. This was clear from the progress made in the firm understanding with the Royal Australasian College of Surgeons which had resulted, as Mr. Beasley had said, in complete reciprocity in the Primary Examinations for the Fellowship. The President also expressed appreciation of His Excellency's references to the contacts with other countries which were kept alive by the frequent exchange of visits. He stated that since the last Hunterian Dinner lectures had been delivered in the College by distinguished teachers from practically all the Dominions, and from the United States and many European countries. The President agreed with Mr. Beasley that Lord Nuffield's gift would provide opportunities which would be unique in the world.

After emphasising the importance of the science as distinguished from the art of surgery the President paid tribute to the memory of John Hunter. He recalled what Lord Horder had said in a memorable Oration before the Hunterian Society : " Let us imagine he is here, as indeed he is, living amongst us in the tradition that he left behind him. Let us be worthy of him, and of it." The President then quoted the following eulogy from Sir James Paget's Hunterian Oration delivered in the College in 1877 : " The influence of such men as Hunter reaches far beyond the time and place of their conscious activity. Their true thoughts live after them. Thus, when we honour the memory of Hunter, we honour not only that which is passed but that which is still present—a still abiding power doing good."

The toast of " The Guests," was proposed by Mr. L. E. C. Norbury, Senior Vice-President, and responded to by His Excellency the High Commissioner for Canada, Mr. Norman Robertson, and by the Vice-Chancellor of the University of London, Professor Lillian Penson.

The toast of "The Hunterian Orator," was proposed by Mr. Zachary Cope, Junior Vice-President, who said :

I rise with pleasure to propose the toast
Of one of whom this College well may boast,
One whom I recollect I first did know
Ten, twenty, thirty, forty years ago,
Who as a friend to me is very dear—
Souttar, Hunterian Orator this year.
A worthy orator, as well you know
Who listened to his words some hours ago
As he most eloquently gave a list
Of what the *great* men saw, but others missed.
But Souttar does not miss much—I recall
He knows the infinitely great and small,
The movements of the atom he can tell
And all the paths of planets just as well,
Draw you the structure of the atom barium
Or plan with equal skill a planetarium,
And revels in those mental acrobatics
Which go with all the higher mathematics.
A famous surgeon he of that great type
Which with fine skill and with experience ripe
Deals safely with the body's every part,
Yea, with the knife can even touch the heart.
Never content with practices outworn
Where'er he touches, there he doth adorn
With instruments, as every case demands
Made at the lathe with his own dextrous hands.
Although no sign of age in him we ken
He must be nearing threescore years and ten.
But judging from his habits I surmise
He keeps quite well by taking exercise
And when he feels the slightest touch of liver
Just takes a boat and rows upon the river ;
With skulls he is a marvel either way
Whether you spell it with a "c" or "k."

He's fond of music and he often brings
Sweet harmony from tightened catgut strings ;
'Tis not surprising that he's thus devoted
For catgut London Hospital is noted.

Though in physique not quite a slender man
I often think of him as Peter Pan,
His most infectious laugh, his merry twinkle,
The eager way he tells the latest wrinkle
Shows us the youthful ever-learning mind
Which to old age will never be resigned.
The toast to you I now will pass
And ask you all to raise your glass
To one whose great ability, amazing versatility
And excellent facility in science and the arts
Whose happy affability and juvenile agility
Just bind him to our hearts.

Mr. Souttar made an amusing speech in reply and finished by recalling the appositeness of George Robey's injunction—"Stop, look and listen," thereby continuing the theme of his Hunterian Oration of that afternoon.

After dinner the Museum was open for the inspection of the guests. An exhibition of Library Treasures, together with the Plans for the rebuilding of the College, were on view in the Council Room.

# OBSERVATIONS ON THE PATHOGENESIS AND TREATMENT OF SKELETAL TUBERCULOSIS

Hunterian Lecture delivered at the Royal College of Surgeons of England

on

17th February, 1948

by

Professor M. C. Wilkinson, M.B., B.S., M.R.C.S., L.R.C.P.

Medical Superintendent, Black Notley Hospital, Essex

I WISH FIRST to consider the part played by the lymphatic and reticulo-endothelial systems in the defence of the body against tuberculosis. The lymphatic glands guard the portals of entry of the body; if these are passed tuberculous bacillæmia occurs, and then it is that the depots of reticulo-endothelial cells in the lungs, liver, spleen, bone marrow, kidneys and serous membranes act as catchment areas for the tubercle bacilli, with the consequence that tuberculous disease is commonly found in these situations.

## TUBERCULOUS LYMPHADENITIS

As the result of primary infection there may or may not develop gross tuberculosis of the lymphatic glands that guard the portal of entry. Two views have been held about the significance of tuberculous lymphadenitis. There are those who, like Marfan (Marfan, A. B., 1931), consider that tuberculosis of a lymphatic gland confers some immunity on a patient; there are others who regard a tuberculous lymphatic gland as a source of danger on the ground that from it tubercle bacilli may leak into the blood stream to cause fresh tuberculous lesions. I have tried to find out which of these views is correct and shall quote for your consideration the evidence that has led me to support Marfan's theory.

During the years 1931-1943 there were admitted to Black Notley 951 children suffering from tuberculous glands of the neck, thorax or abdomen, the majority of whom had severe adenitis, for which treatment in a sanatorium was considered necessary. Some of these patients have been followed up and the findings are shown in Tables I and II. It will be seen that these patients with few exceptions developed no other lesion and must be considered to have developed an immunity.

TABLE I

*Follow-up of 98 children admitted for the treatment of tuberculous thoracic glands.*

| Duration of follow-up in years | Number of Patients | Number of Patients well | Number of Patients not well |
|---|---|---|---|
| 1 | 2 | 1 | 1 (died miliary tuberculosis) |
| 2 | 4 | 4 | 0 |
| 3 | 5 | 5 | 0 |
| 4 | 10 | 9 | 1 (developed phthisis) |
| 5 | 16 | 16 | 0 |
| 6 | 11 | 11 | 0 |
| 7 | 15 | 15 | 0 |
| 8 | 6 | 6 | 0 |
| 9 | 8 | 8 | 0 |
| 10 | 6 | 6 | 0 |
| 11 | 6 | 6 | 0 |
| 13 | 5 | 5 | 0 |
| 14 | 1 | 1 | 0 |
| 15 | 1 | 1 | 0 |
| 16 | 2 | 2 | 0 |
| | 98 | 96 | 2 |

Table I endorses the view that the children treated for tuberculous thoracic glands, in many cases severe, developed immunity. Except for the instances noted, no fresh tuberculous lesions developed in any of the patients.

TABLE II

*Follow-up of 297 patients treated at Black Notley for tuberculous cervical adenitis: 244 patients were aged 14 years or under, and 53 were over 14*

| Duration of follow-up in years | Number of Patients | Number of Patients well | Number of Patients not well |
|---|---|---|---|
| 1 | 43 | 42 | 1 (died miliary tuberculosis) |
| 2 | 65 | 65 | 0 |
| 3 | 57 | 57 | 0 |
| 4 | 58 | 58 | 0 |
| 5 | 45 | 45 | 0 |
| 6 | 16 | 16 | 0 |
| 7 | 11 | 11 | 0 |
| 9 | 1 | 1 | 0 |
| 13 | 1 | 1 | 0 |
| | 297 | 296 | 1 |

One patient, aged 17 years, found to have healed apical pulmonary tuberculosis on follow-up.

Follow-up reports of patients admitted for the treatment of tuberculous abdominal glands showed the same results.

Most of the patients admitted for tuberculous lymphadenitis were children, the period of life when, according to Harris and others (Harris, J. A., Jackson, C. M., Paterson, D. G. and Seaman, R. E., 1930), the lymphatic tissues reach their peak of activity. After puberty the

lymphoid tissues wane, at first rapidly, then more slowly. Therefore it would be expected that tuberculous lymphadenitis, when it occurs in association with skeletal tuberculosis would occur most frequently in children, and would have a beneficent effect on the disease (Tables III, IV, V).

TABLE III

*Incidence of associated tuberculous lymphadenitis in 386 children and adults with skeletal tuberculosis admitted in the period* 1938-1947

| | | |
|---|---|---|
| Age 14 years and under (Total patients 123) | | |
| Patients with associated tuberculous lymphadenitis | 46 | (37.4%) |
| Patients with no evidence of adenitis | 77 | (62.6%) |
| Over 14 years of age (Total patients 263) | | |
| Patients with associated tuberculous lymphadenitis | 16 | (6.1%) |
| Patients with no evidence of adenitis | 247 | (93.9%) |

Radiographs of the lungs were available for the whole group of 386 patients referred to in this Table. Radiographs of the abdomen were available in only a proportion of them. The Table therefore shows all patients with cervical and thoracic adenitis and a proportion with abdominal adenitis.

TABLE IV

*Patients suffering from skeletal tuberculosis, either with or without associated tuberculous glands, grouped according to severity of the disease*

| | Number of patients | Good Resistance | Disease Moderate | Disease Severe |
|---|---|---|---|---|
| Age 14 years and under | | | | |
| With tuberculous lymphadenitis | 46 | 18 (39.1%) | 23 (50.0%) | 5 (10.9%) |
| No tuberculous lymphadenitis | 77 | 6 (7.8%) | 55 (71.4%) | 16 (20.8%) |
| Age over 14 years | | | | |
| With tuberculous lymphadenitis | 16 | 7 (43.75%) | 7 (43.75%) | 2 (12.5%) |
| No tuberculous lymphadenitis | 247 | 9 (3.6%) | 176 (71.3%) | 62 (25.1%) |

This Table shows the beneficent effect of tuberculous lymphadenitis on resistance.

TABLE V

*Distribution by age groups of patients admitted from* 1938 *to* 1947 *with skeletal tuberculosis and associated lesions in the lungs, skeleton, kidneys or abdomen. The Table excludes patients with associated lymphadenitis only. For most of the patients radiographs of the chest were available*

| Age Group | Total Number of Patients | Number of Patients with associated tuberculous lesions | Percentage |
|---|---|---|---|
| 0—5 | 100 | 14 (including 4 cases of tuberculous meningitis) | 14.0 |
| 6—10 | 88 | 8 (including 3 cases of tuberculous meningitis) | 9.1 |
| 11—15 | 43 | 8 | 18.6 |
| 16—20 | 73 | 30 | 41.09 |
| 21—25 | 62 | 35 | 56.5 |
| 26—30 | 44 | 23 | 52.3 |
| 31—40 | 45 | 24 | 53.3 |
| 41—50 | 41 | 19 | 46.3 |
| 51—60 | 17 | 12 | 70.6 |
| 61—over | 4 | 0 | nil |
| | 517 | | |

This Table shows the increased percentage of associated lesions after puberty when there is waning of lymphoid tissue.

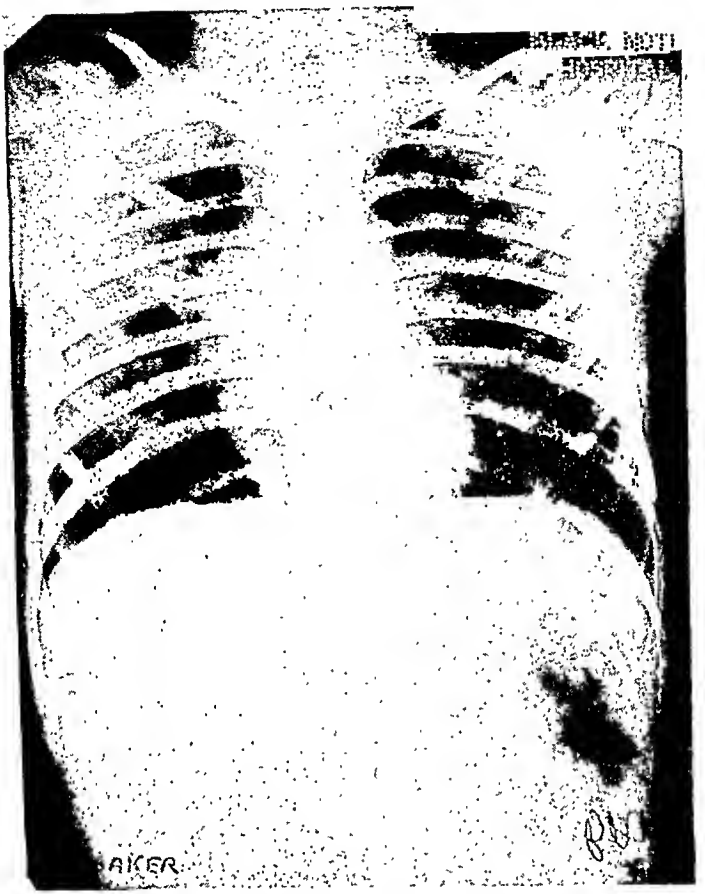


Fig. 1. Resolving right hilum adenitis, in child who also had tuberculous hip, and tuberculous epididymitis. (T.B. present in pus from epididymis.)

Fig. 2. Tomograph of hip of same child after 18 months' treatment. Circumscribed cavity seen in femoral neck. Child now ambulant ; hip mobility good.

The low incidence of tuberculous adenitis associated with skeletal tuberculosis in adults can be compared to a similar low incidence associated with pulmonary tuberculosis in adults, namely 3 per cent. (Wilkinson, M. C., and Cureton, R. J., 1943). This figure corresponds with that given by Osler (Osler, W., 1920) for the presence of tuberculous adenitis in 2,000 patients who had died of pulmonary tuberculosis and who were examined post-mortem.

## TUBERCULOUS BACILLÆMIA

The reticulo-endothelial cells of the lymph gland strain off, not by a mechanical but by a vital action, the bacilli entering from the portal of primary infection. The two components of the lymph gland, the lymphocytes and the reticulo-endothelial cells, are found wherever a focus of tuberculosis develops in the body. According to Besredka (Besredka, A., 1927) the tissues of the body have receptor cells in which organisms become localised irrespective of their route of entry. For tubercle bacilli the receptor cells are those of the reticulo-endothelial system. The disease occurs most frequently wherever in the body there are reticulo-endothelial depots; especially are the reticulo-endothelial cells of the lungs activated by the tubercle bacillus. Experimental confirmation of this view has been offered by Coulaud (Coulaud, E., 1933), who demonstrated tuberculosis in the lung following a sub cutaneous injection of tubercle bacilli, and Rosenthal (Rosenthal, S. M., 1936 and 1937), who found that following either oral administration or subcutaneous injection of B.C.G., there were reticulo-endothelial reactions in the lungs, liver, spleen, and kidneys. The following clinical record tends to the same conclusion:

A child, aged six, under treatment for severe tuberculosis of the hip, developed a sub-acute miliary tuberculosis. This gradually increased in intensity, as seen in serial X-rays of the lungs, until at the end of three months she developed tuberculous meningitis and died. At autopsy miliary lesions were found in the lungs, and to a lesser extent in the liver, spleen, kidney and peritoneum. No tuberculous glands were found in the body. The bone marrow was not examined for miliary tubercles, but work recently published by Schleicher (Schleicher, E. M., 1946) suggests that they must have been present for he found tubercles in the sternol marrow of every one of a series of patients with terminal miliary tuberculosis, and suggested examination of the sternol marrow for the diagnosis of early miliary tuberculosis. The reticulo-endothelial depots of the marrow are situated at the metaphyseal ends of the long bones, and it is here precisely that the original foci of skeletal tuberculosis occur. Following a bacillæmia, therefore, skeletal tuberculosis may start in the metaphyses of the long bones. It might be expected also from the distribution of the reticulo-endothelial depots that skeletal tuberculosis would be only one feature of a disseminated disease and that other tuberculous lesions would frequently occur in the same patient. That this is true may be seen from Table VI.

TABLE VI

*Incidence of skeletal tuberculosis with or without associated lesions, exclusive of tuberculous adenitis, in patients discharged during the period 1935-October, 1947*

| Site of skeletal lesion | Age 14 years and under | | Over 14 years | | Total | | Total |
|---|---|---|---|---|---|---|---|
| | Without associated lesions | With associated lesions | Without associated lesions | With associated lesions | Without associated lesions | With associated lesions | |
| | | | | | | % | |
| Spine | 49 | 14 | 80 | 76 | 129 | 90 (41.1) | 219 |
| Hip | 78 | 8 | 24 | 12 | 102 | 20 (16.4) | 122 |
| Knee | 42 | 3 | 16 | 21 | 58 | 24 (29.3) | 82 |
| Ankle and Foot | 11 | 0 | 11 | 16 | 22 | 16 (42.1) | 38 |
| Shoulder | 1 | 0 | 6 | 2 | 7 | 2 (22.1) | 9 |
| Elbow | 3 | 0 | 0 | 4 | 3 | 4 (57.1) | 7 |
| Wrist | 2 | 1 | 2 | 7 | 4 | 8 (66.7) | 12 |
| Sacro-Iliac | 5 | 0 | 5 | 10 | 10 | 10 (50.0) | 20 |
| Sterno-Clavicular | 0 | 0 | 1 | 1 | 1 | 1 (50.0) | 2 |
| Pubis | 0 | 0 | 0 | 2 | 0 | 2(100.0) | 2 |
| Tuber Ischii | 0 | 0 | 2 | 1 | 2 | 1 (33.3) | 3 |
| Dactylitis | 0 | 1 | 0 | 0 | 0 | 1(100.0) | 1 |
| Totals | 191 | 27 | 147 | 152 | | | 517 |

The presence of associated lesions, exclusive of tuberculous adenitis, was much greater in adults than in children.

## STEROLS AND RETICULO-ENDOTHELIAL ACTIVITY

If it is accepted that resistance to tuberculosis is effected through the lymphatic and reticulo-endothelial tissues, then the relation of sterols to reticulo-endothelial activity becomes a matter of great importance. There are good reasons for believing that increased sterol formation in the tissues calls into action the great phagocytic function of the reticulo-endothelial system. Fraser (Fraser, J., 1935) has commented on this matter in relation to skeletal lipoid granulomatosis, a condition in which there is a disordered stimulation of reticulo-endothelial tissue due to excess of sterol. Fontana (Fontana, P., *et al*, 1929) observed a reticulo-endothelial response in rabbits fed on large amounts of vio-sterol. This view can, in my opinion, be confirmed by clinical observation. At Black Notley we have a maternity unit for tuberculous mothers, many of whom have been confined while suffering from pulmonary tuberculosis, others from skeletal tuberculosis. We have found that tuberculous mothers can safely tolerate pregnancy—a state in which the blood cholesterol is higher than normal—in spite of the additional strain they have to undergo. It is noteworthy also that among contacts with tuberculosis the marital contacts form a relatively immune group—a fact of particular interest in view of the probability that in the married there is increased formation of sex hormones, which are also sterols. Heliotherapy and ultra violet irradiation of the skin, in my opinion useful measures in the treatment of skeletal tuberculosis, result in the formation of calciferol, yet another

sterol; and recently this substance has been used successfully in the treatment of lupus. Such observations open a wide field for further investigation, not only of sterol metabolism and reticulo-endothelial cell activity, but also of sterol metabolism and lymphopoiesis, for Fontana and his colleagues note that cholesterol is present in lymphoid tissue.

### Reticulo-endothelial activation by Tuberculous antigens

The experimental work of Rosenthal on the activation of the reticulo-endothelial tissues by the use of B.C.G. as a specific antigen has already been quoted. He reports that the introduction of B.C.G. into guinea-pigs produces a local specific response with the formation of tubercles and a generalised non-specific reaction of the reticulo-endothelial system. In the human subject this specific stimulus may also be provided by auto-inoculation; and on this conception is based the operative treatment devised by Robertson-Lavalle (Robertson-Lavalle, C., 1942).

Robertson-Lavalle drills holes into certain foci in tuberculous bone and claims that tuberculous toxins are thereby released into the tissues with benefit to the patient's powers of resistance. Support of a more general character comes from the observation, which I am able to substantiate, that improvement in a patient's general condition frequently follows operation into tuberculous bone. Norman Dott reports improvement in the patient's general condition following his operation of anterior decompression for Pott's paraplegia, an operation by which tuberculous bone is opened up. A beneficial effect follows laparotomy for tuberculous peritonitis; nephrectomy for tuberculosis of the kidney is followed by improvement in the opposite kidney; and after removal of one Fallopian tube the opposite one usually improves. These effects may be due to drainage of tuberculous tissues, removal of tuberculous foci, auto-inoculation, or a combination of all three.

The theory of a post-operative auto-inoculation is favoured by the poor results which follow amputation of tuberculous limbs. Thus, of 12 patients with skeletal tuberculosis who were treated by amputation before or after admission to Black Notley, five later developed tuberculous lesions and of these two died; two others died, one possibly from a non-tuberculous condition; one is known to have done well; and of four all trace has been lost. Amputation of a tuberculous limb may be compared with orchidectomy for tuberculous epididymo-orchitis, an operation which has frequently been the prelude to admission for the treatment of tuberculosis of other organs.

Finally, the view that operation is followed by a beneficial auto-inoculation can be supported by a comparison of end results in two groups of patients with multiple tuberculous lesions—those who have been treated by operation and those who have not. One such study is summarised in Table VII.

TABLE VII

*Comparison of follow-up results in two similar groups of patients suffering from multiple tuberculous lesions, one treated with and the other without operation. Both groups received similar constitutional treatment. Operation was into tuberculous tissues; incision of abscesses is excluded*

| | Total Number | Result | | | |
|---|---|---|---|---|---|
| | | Good | Moderate | Poor | Death |
| Moderately severe disease treated by operation | 35 | 29 (82.8%) | 5 (14.3%) | 1 (2.8%) | 0 |
| Moderately severe disease treated without operation | 66 | 50 (75.5%) | 6 (9.2%) | 3 (4.6%) | 7 (10.6%) |
| Very severe disease treated by operation | 14 | 7 (50.0%) | 2 (14.3%) | 3 (21.4%) | 2 (14.3%) |
| Very severe disease treated without operation | 14 | 3 (21.4%) | 1 (7.1%) | 3 (21.4%) | 7 (50.0%) |

## GENERAL PRINCIPLES OF TREATMENT

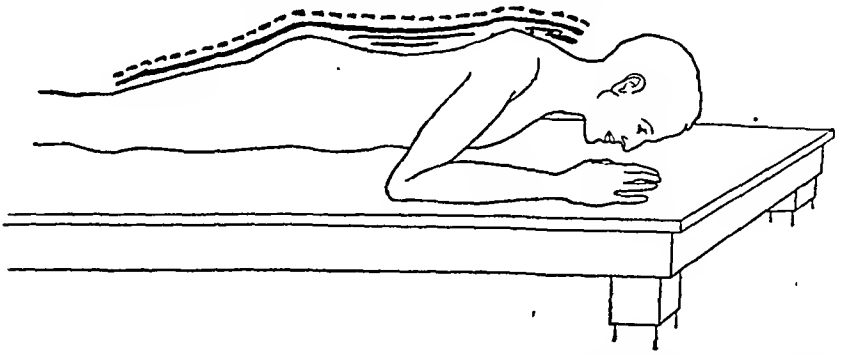
All the operative treatment mentioned in this Paper has been based on thorough constitutional treatment. It is necessary only to refer with gratitude to the work of Calvé, Rollier, Gauvain, Robert Jones, Pugh, Girdlestone and the whole school of British Orthopædic surgeons who established this principle in the treatment of skeletal tuberculosis. Splintage of my patients has been as little as possible compatible with efficiency, so that muscle spasm is relieved, the joint rested, and muscle tone and the general nutrition of the patient maintained. Rigid immobilisation, except in the early treatment of tuberculosis of the spine, has not been sought. No patient has been observed to develop a renal calculus. Weight-bearing as soon as the disease is quiescent is encouraged.

## TUBERCULOSIS OF THE SPINE

I should now like to turn from the general to the particular and to consider the disease as it occurs in each part of the skeleton. During the years 1931-1947, 340 patients were discharged from Black Notley after treatment for tuberculosis of the spine—more than twice as many adults were affected than children. Nearly 50 per cent. of the adults had associated tuberculous lesions, not including tuberculous lymphadenitis. There were eight deaths from tuberculous meningitis in children with tuberculous spines. The chief cause of death in adults suffering from tuberculosis of the spine were chronic suppuration, pulmonary tuberculosis and uræmia. So tuberculosis of the spine is an especially severe form of skeletal tuberculosis.

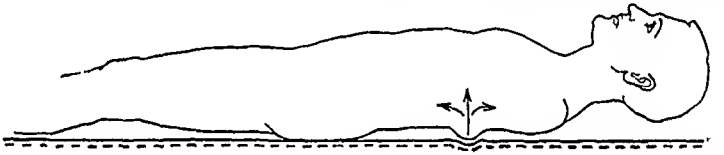
Treatment must be early to ensure success, and the aim must be to limit the disease to those vertebral segments affected when the patient is admitted. I have devised a special type of plaster bed for this purpose. By following the principles of Goldthwaite, who remoulded static deformities of the back by plaster beds, I have been able to effect distraction and immobilisation of the diseased vertebral bodies while the patient lies in a natural position. Thus the destructive process is prevented from spreading to adjacent vertebral bodies.

The patient is laid on his face and pieces of felt are stepped up above and below the hump until a level surface is produced. A piece of felt is then placed over all and cut and moulded to fit (Fig. 3), the plaster is then applied with much moulding. When the plaster is set, the pieces



*By kind permission of the Royal Society of Medicine.*

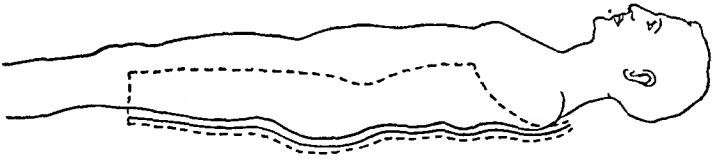
Fig. 3. Patient prone with felt pads, superficial layer of felt, and layer of plaster in place.



*By kind permission of the Royal Society of Medicine.*

Fig. 4. Patient on back, with additional felts removed.

of felt are removed; the patient's back becomes accommodated to the shape of the plaster and distraction of the affected segments occurs (Figs. 4 and 5). The appearance of the bed is seen in the illustrations (Figs. 6 and 7).



*By kind permission of the Royal Society of Medicine.*

Fig. 5. Patient on back, with back moulded into shape of plaster.

When recalcification starts, a well-moulded plaster bed is made without distraction of the affected vertebræ, so that collapse and consolidation are encouraged. Compensatory curves are found to develop naturally when the patient gets up. A light spinal brace is worn until the spine seems stable.

A follow-up of patients treated for tuberculosis of the spine shows that a high proportion eventually heal by bone fusion or stable fibrous ankylosis. 131 follow-up reports were received in which there was X-ray or strong presumptive evidence of the type of ankylosis present. 80 of these patients had bony or stable fibrous ankylosis; 51 had unstable

Fig. 6. Plaster bed to show the moulding and how the shoulders are dropped back in their natural position. This patient had had a posterior fusion.

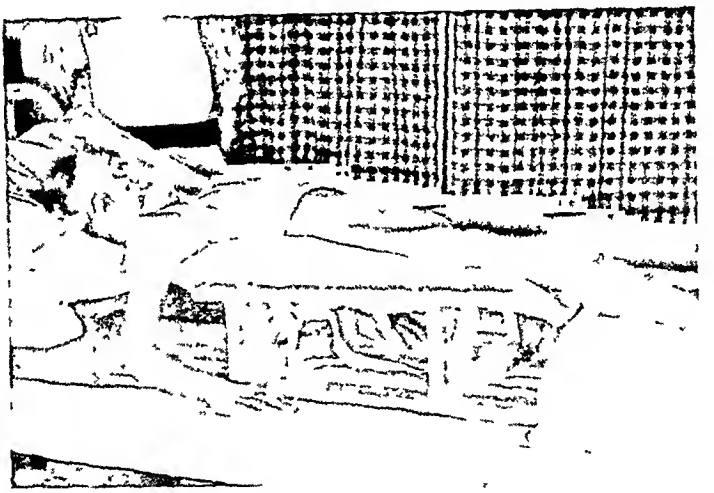


Fig. 7. Another view of the same plaster bed.

fibrous ankylosis. Of the patients with unsound ankylosis, nine had been admitted with gross vertebral destruction due to old-standing disease. A total of 65·6 per cent. of the patients treated originally at Black Notley obtained a stable spine by constitutional treatment only. Some guidance concerning prognosis is, therefore, necessary to enable the surgeon to select patients for posterior fusion. The extent of the vertebral damage affords the most important clue because bony or strong fibrous fusion is improbable if three or four vertebral bodies have been badly damaged. The degree of vertebral destruction depends, other things being equal, on the locality of the disease and the age of the patient. The following Table shows results compiled on this basis:

TABLE VIII

*Results of constitutional treatment of tuberculosis of the spine in* 131 *patients*

| Locality affected | Stable or bone ankylosis | | | Fibrous and unstable ankylosis | | |
|---|---|---|---|---|---|---|
| | 14 years and under | Over 14 years | Total | 14 years and under | Over 14 years | Total |
| Lumbo-Sacral | 1 | 3 | 4 | 0 | 1 | 1 |
| Lumbar Spine | 12 | 24 | 36 | 3 | 7 | 10 |
| Dorso-Lumbar | 3 | 14 | 17 | 5 | 5 | 10 |
| Lower and Mid-Dorsal | 7 | 13 | 20 | 12 | 16 | 28 |
| Upper Dorsal | 1 | 0 | 1 | 1 | 0 | 1 |
| Cervical | 1 | 1 | 2 | 1 | 0 | 1 |
| | 25 | 55 | 80 | 22 | 29 | 51 |

Stability of the spine after constitutional treatment occurred in 53.3 per cent. of the children and 65.5 per cent. of the adults. The mid- and lower dorsal areas are the most vulnerable.

Average duration of follow-up : Of patients with bony ankylosis .. .. 5.4 years
Of patients with stable fibrous ankylosis .. 5.0 years
Of patients with unstable fibrous ankylosis 4.0 years

From this Table it is seen that the mid- and lower dorsal areas of the spine require fusion more often than others. It has been said that spinal bone grafts in children will not prevent deformity, but I think they may modify it. Sometimes, however, chronic sluggish disease will persist in spite of good posterior fusion.

Multiple lesions in the vertebral column are common in tuberculosis of the spine, either as clinical lesions or as calcified vacuoles seen in the vertebral bodies in the follow-up X-rays (Fig. 8). Probably the whole spinal column is inseminated with tubercle bacilli at the time of blood stream infection. It is advisable, therefore, to limit the extent of a spinal graft to one vertebral body above and below the principal lesion. Otherwise the mobility of the spine is so much impaired that considerable stress falls on the junction between the grafted and non-grafted parts, causing sometimes a fresh lesion at this site.

The hæmatagenous insemination of the vertebral bodies may occur through the perivertebral plexus or veins, described by Batson (Batson, O.V., 1940, *Ann. Surg.*, **112**, 138), which has ramifications into the base of the brain and on to the anterior surface of the chest wall. These ramifications would account for the special association of tuberculous meningitis with spinal tuberculosis in the child, and for the common association of a superficial tuberculous abscess of the chest wall with spinal tuberculosis in the adult.

Operations on tuberculous vertebræ have not been practised in this series except for patients with paraplegia. owing to the risk of tuberculous meningitis. Two out of five patients who had operation on vertebral bodies for tuberculous paraplegia developed meningitis. Nevertheless, if operation were safe, it would be desirable to operate on the vertebral bodies for tuberculous disease, at a suitable stage in the illness, not only for the beneficial local effect, which can be seen following operations

on the bodies for paraplegia, but also for any benefit to associated lesion that might result from auto-inoculation. The advent of streptomycin would render such operations safe and in that event the operative treatment of tuberculosis of the spine may become desirable.

Fig. 8. Multiple tuberculous lesions in the spine of a child.

## TUBERCULOSIS OF THE HIP

Unlike tuberculosis of the spine, tuberculosis of the hip occurs more often in the child than the adult. 194 patients were treated during the years 1930-1946; more than a third of these were admitted before they were six years old, and more than half before they were 11. Only

16·4 per cent. of patients had associated tuberculous lesions, exclusive of tuberculous lymphadenitis. The prognosis for tuberculosis of the hip, treated conservatively, would, therefore, be satisfactory if a stable hip could be obtained, but in a series which I investigated (Wilkinson, M. C., 1942) 22 patients out of 50 had an unstable hip after conservative treatment. In children of tender years major stabilisation operations may be unsafe ; and the bones are still very cartilagenous and unsuitable for bone grafting operations : if a child has to wait until he is older for a fusion operation, he may be handicapped physically during much of his childhood. I have, therefore, used a displacement osteotomy to short-circuit the joint and allow early weight-bearing, and have found that natural fusion of the joint frequently follows. Moreover, such an osteotomy may be performed to accelerate healing of the disease (Figs. 9 and 10).

The benefit from displacement osteotomy may be due either to relief from shearing stresses or to an ischæmic effect in the femoral head and neck following division of vessels : thus an ununited fracture of the neck of the femur will unite following a MacMurray osteotomy. In tuberculosis of the hip the osteotomies that I have performed have often been into tuberculous tissue, with consequent drainage of tuberculous bone and possibly beneficent auto inoculation of the patient.

Bony fusion across the diseased joint following displacement osteotomy may take several years to become established, and during the earlier

Fig. 9. Unstable ankylosis : quiescent disease.

Fig. 10. Ten years after displacement osteotomy.

part of this time the patient should wear a well-moulded celluloid splint. For this reason in a series of patients I have taken a graft from the outer and upper aspect of the femoral shaft and great trochanter before performing the osteotomy: the osteotomy is then performed, after which the trochanter is elevated and a channel is gouged along the upper surface of the femoral neck into the ilium; the graft is driven home along the channel. As Telford remarks (Telford, E. D., and Geddes, J. E., 1943), the curve of this graft fits the upper concave surface of the femoral neck (Figs. 11, 12 and 13). The graft is frequently inserted into areas where there has been or is tuberculous disease; it may be absorbed but acts as a source of osteogenesis, facilitating reossification of the diseased area.

Displacement osteotomy, with or without a graft, has been used for the treatment of active disease when a suitable degree of resistance is reached. In the child it is advisable to delay the operation until recalcification is beginning; in the adult displacement osteotomy may be performed after 12 months' preliminary constitutional treatment: in the child 18 months or more is required. An abscess may be encountered at operation, but with the good constitutional treatment available at Black Notley no patient has developed a permanent sinus, or run more than a moderate temperature for 10 days after operation. Displacement osteotomy has also been used for the treatment of chronic secondary infection of the hip, and in three cases out of five the sinuses, previously intractable, have healed completely.

Fig. 11. Unsound ankylosis of tuberculous hip.

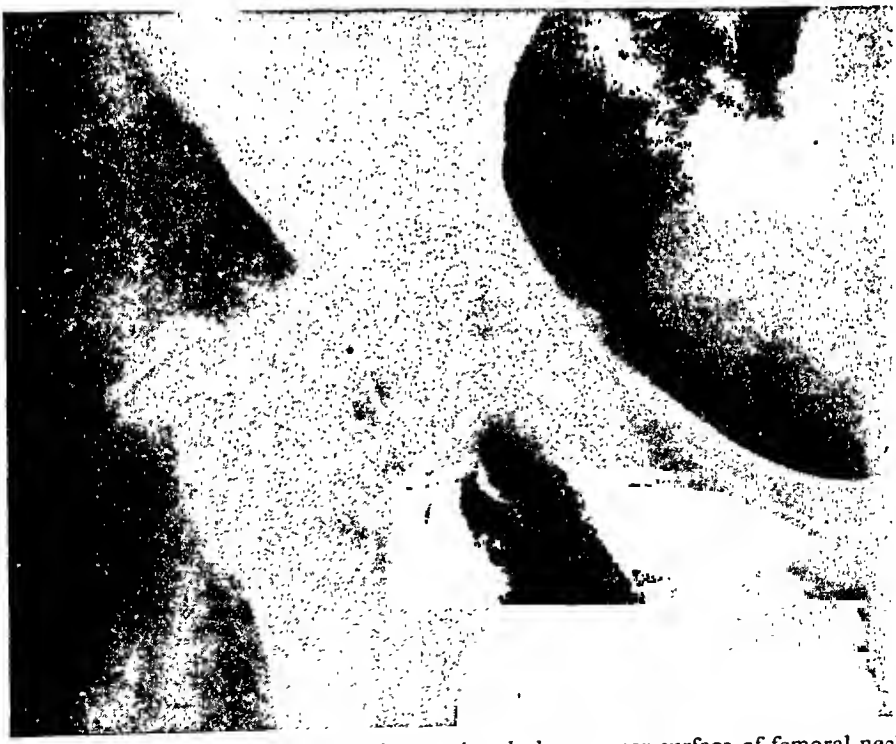


Fig. 12. Osteotomy and graft from femur placed along upper surface of femoral neck into ilium.

Fig. 13. Stable hip with bone fusion 15 months afterwards.

Fig. 14. Tuberculous hip in a child, still active after two years' conservative treatment.

Fig. 15. Same hip, three months after sequestrectomy.

Fig. 16. Four years later ; unsound ankylosis : quiescent disease

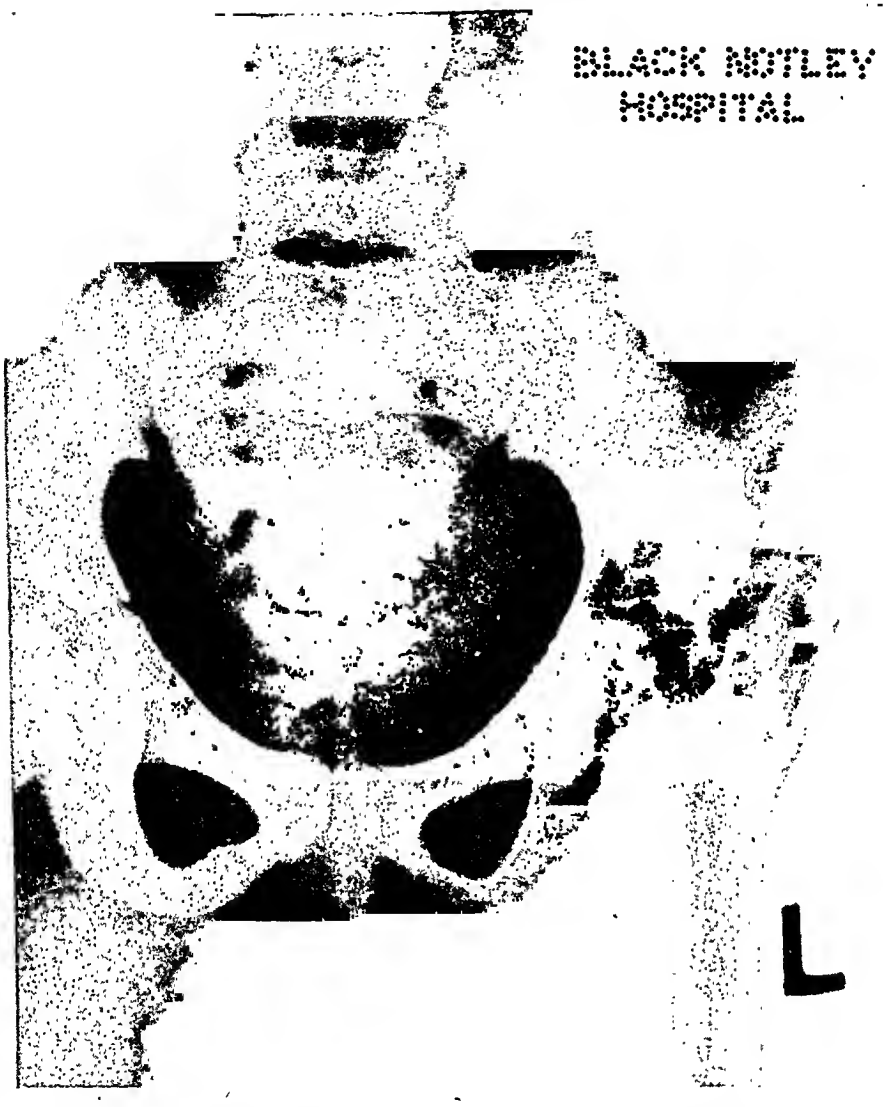



Fig. 17. Five months after displacement osteotomy and graft. The graft has cracked but the hip is fusing and is stable. Child ambulant.

Finally, in a small series of patients benefit has been obtained by the curettage of tuberculous foci in the hip joint or its neighbourhood (Figs. 14, 15, 16 and 17), accompanied in two patients by the use of bone chips. Several patients have also benefited by osteotomy through diseased areas without displacement. The operations described are safe and apart from one anæsthetic death no anxiety has been encountered.

## TUBERCULOSIS OF THE KNEE

One hundred and eighteen patients were discharged after treatment for tuberculosis of the knee during the years 1931-October, 1947. Of these 56·8 per cent. were children and 43·2 per cent. were adults. Of the

patients over 14 years 66.6 per cent. had associated tuberculous lesions, excluding tuberculous lymphadenitis; a high proportion of these lesions were in the lungs; a special feature of tuberculosis of the knee in the young adult is the tendency to develop associated pulmonary tuberculosis.

In my experience the results of conservative treatment in children have been good. The younger children in particular often recover with a useful range of movement of the knee, a result due, I believe, to the fact that the growing ends of the femur and the tibia in the young child include a large amount of cartilage—a matrix in which caries does not spread easily nor infection fall heavily. Even when cartilage has been partially destroyed there may be a good range of movement; this was seen in a girl who later developed pulmonary tuberculosis of which she died and whose knee was examined at autopsy.

Children whose joint space was destroyed by disease were not treated by excision. Though eminent authorities have recommended this operation in children, I have been impressed by Harris's observation (Harris, H. A., 1933), that trauma even in the neighbourhood of an epiphysis may promote premature fusion of that epiphysis: also I have found that many children whose knee joint has been destroyed by tuberculosis will develop a stable knee eventually if a well-moulded celluloid splint is worn for a sufficient time.

Excision of the knee for tuberculosis in the adult has been generally accepted as a useful operation, even though disease may still be present at the time of the operation. 44 of the adult patients discharged during the years 1931-October, 1947, in this series were treated by excision, after preliminary constitutional treatment. The late results have been almost uniformly satisfactory, not only for the knee but also for associated lesions (Figs. 18, 19, 20 and 21).

## TUBERCULOSIS OF THE FOOT AND ANKLE

From 1937-October, 1947, 57 patients suffering from tuberculosis of the foot and ankle have been admitted to Black Notley. The localisation of tuberculous lesions in this region is affected by the age of the patient, which is not surprising in view of the fact that the degree of ossification of the tarsal bones also depends on age. The centres of ossification for the shafts of the metatarsals appear earliest, then the centres for some of the tarsal bones, and last the centres for the lower ends of the tibia and fibula. Tuberculous bacillæmia, occurring in early infancy, therefore, selects the metatarsal bones; in early childhood it is usual to see tuberculosis of the tarsal bones; in later childhood and in adult life tuberculosis of the ankle becomes the commonest type of tuberculosis of the foot. The bone of the foot most often affected in my series was the astragalus, and this is the site of the earliest lesion in tuberculosis of the ankle, so that very often the sub-astragaloid joint as well as the ankle joint is affected. Another form of tuberculosis of the foot less frequently found is astragalo-scaphoid tuberculosis.

Fig. 18. Active disease of knee before excision.

Fig. 19. Active pulmonary tuberculosis in same patient (T.B. +).

Fig. 20. Fusion of knee seven years after excision.

Fig. 21. Soundly healed pulmonary disease at same date.

In children the lesions are usually solitary; in adolescents and adults in this series more than half the patients had associated lesions, exclusive of tuberculous lymphadenitis. The commonest associated lesion was pulmonary tuberculosis.

In my experience the results of constitutional treatment for tuberculosis of the foot are good: in adults I believe that constitutional and operative treatment should be combined. I do not regard amputation as suitable. 27 of 54 patients were treated by operation for disease of the tarsal bones, astragalo-scaphoid joint, or ankle joint: only three of these were children. Two of these, both young adult females, later developed pulmonary tuberculosis from which they appear to be making a satisfactory recovery. One patient died of multiple lesions, and one is still under treatment. The essential part of the operative treatment has been curettage of the diseased bone, usually the astragalus, with, in the case of the ankle joint, the removal of the synovial membrane. A graft has been slid down from the tibia into the astragalus in some cases. Miss Forrester-Brown (Forrester-Brown, M., 1939) has claimed good results from a similar operation.

## TUBERCULOSIS OF THE SHOULDER

There have only been 13 patients with tuberculosis of the shoulder between 1931-October, 1947: three of these were children. Three of the 10 adults had associated pulmonary tuberculosis, and one had associated tuberculosis of the elbow. Treatment was by constitutional measures for all patients, and for seven of the adults by operation. The disease, in my opinion, starts in the humeral head and, therefore, any operation which involves the head of the humerus must result in opening up diseased areas therein. Six of these patients, all adults, were treated by arthrodesis, by turning down the acromion process and inserting it into a slot in the head of the humerus, after the manner described by Watson-Jones (Watson-Jones, R., 1933). The results were uniformly good: in one patient two large sequestra had to be removed from the head of the humerus at operation (Fig. 22). No operation was required for the three children of whom two were found to have bony ankylosis on follow-up.

## TUBERCULOSIS OF THE ELBOW

Twenty patients during the years 1931-October, 1947, were discharged after treatment for tuberculosis of the elbow. Six were children and 14 adults: eight of the adults had associated pulmonary tuberculosis; three adults and one child had associated skeletal tuberculosis. Tuberculosis of the elbow in my opinion usually starts in the olecranon process of the ulna. All patients were treated by thorough constitutional measures: a modified excision was performed for six of the adults and is now always performed for adults after preliminary constitutional treatment. The approach is a posterior one. Osteotomy of the olecranon is performed to aid exposure of the joint: the olecranon is resutured

Fig. 22. Insertion of acromion into cavity remaining after removal of sequestra from humeral head note healed apical pulmonary lesions.

after the joint has been excised. The disease is usually mainly synovial and very little bone has to be removed; the attachment of the biceps tendon is not included in the operation area. The elbow is splinted with a plaster or celluloid splint for a year after operation; a small but useful range of movement has resulted in all six patients operated on.

## TUBERCULOSIS OF THE WRIST

Nineteen patients were treated at Black Notley for tuberculosis of the wrist between 1931-October, 1947: four were children and 15 adults. 11 of the adults had associated tuberculous lesions, exclusive of tuberculous lymphadenitis: indeed associated tuberculous lesions in other parts of the skeleton and in the lungs were especially common with this condition. More than ever the prognosis depends on the progress of the associated tuberculous lesions.

Tuberculosis of the wrist usually starts in the carpo-metacarpal range of joints. The carpal bones are gradually invaded and finally the wrist joint. Constitutional treatment is essential and an important point to note is that splintage must include the wrist and carpo-metacarpal joints yet ensure a full range of movement at the metacarpo-phalangeal joints. If it does not, permanent disability of the hand will follow. Operation for tuberculosis of the carpus is also performed when a degree of resistance has been established. A dorsal incision is made over the carpus, the diseased areas curetted and sequestra removed. A considerable proportion of the carpal bones can be removed by curettage without impairing the stability of the wrist. A small range of movement usually results when the disease has become quiescent. This operation was performed in five patients in this series. Two of these patients subsequently developed associated lesions, one in the spine and peritoneum, the other in the spine and epididymes: there has been, apparently, a full recovery in both patients, one of whom has been well for seven years.

---

I wish to acknowledge my indebtedness to Sir Heneage Ogilvie for his encouragement; to many orthopædic surgeons for their teaching; to the Essex County Council and the Chief Tuberculosis Officer, Dr. W. A. Bullough, for the opportunities they have offered; to Mr. S. L. Higgs, Consulting Surgeon for Surgical Tuberculosis to the Essex County Council, and to Mr. R. Reid, Consulting Surgeon to the Essex County Council, for constant helpful advice; to Dr. Franklin G. Wood, Consulting Radiologist to the Black Notley Hospital, and to Miss Slater, the Radiographer, for the X-rays; to Dr. Jack Dixon for the high standard of anæsthesia employed; to Dr. Maurice Newfield for helpful criticism of the manuscript; and, not least, to the Matron, Miss M. Ruck, and the nursing staff, who, through their devotion to duty, have given the constant attention to detail which is necessary for the treatment of patients suffering from skeletal tuberculosis.

---

## REFERENCES

BATSON, O. V. (1940) *Ann. Surg.* 112, 138.
BESREDKA, A. (1927) *Local Immunisation.* London.
COULAUD, E. (1933) *Rev. Tuberc., Paris* 1, 819.

FONTANA. P., MIMILLA, A. and COLLEAGO, J. A. (1929) *An. Fac. Med., Montevideo* **14**, 1075.
FORRESTER-BROWN, M. (1939), *Proc. Roy. Soc. Med.* **33**, 149.
FRASER, J. (1935) *Brit. J. Surg.* **22**, 800.
HARRIS, H. A. (1933) *Bone Growth in Health and Disease.* London.
HARRIS, J. A., JACKSON, C. M., PATERSON, D. G., and SEAMAN, R. E. *The Measurement of Man.* Univ. of Minnesota Press, Minneapolis, 1930.
MARFAN, A. B. (1931) *Maladies de la Premiere Enfance.* Paris, p. 441.
OSLER, W. (1920) *Principles and Practice of Medicine.* London, p. 175.
ROBERTSON-LAVALLE, C. (1942) *Biological Surgery in Tuberculosis.* Buenos Aires.
ROSENTHAL, S. M. (1936) *Arch. Path.* **22**, 348.
——————— (1937) *Ann. Inst. Pasteur* **58**, 652.
SCHLEICHER, E. M. (1946) *Amer. Rev. Tuberc.* **53**, 115.
TELFORD, E. D., and GEDDES, J. E. (1943) *Brit. J. Surg.* **30**, 189.
WATSON-JONES, R. (1933) *J. Bone Jt. Surg.* **15**, 862.
WILKINSON, M. C. (1942) *Non-Pulmonary Tuberculosis.* London, p. 91.
——————— and CURETON, R. J. (1943) *Lancet* **2**, 662.

# THE SURGICAL RELIEF OF ABDOMINAL PAIN BY SPLANCHNIC BLOCK

The Substance of a Lecture delivered at the Royal College of Surgeons of England

on

4th May, 1948

by

Professor Dr. Miguel Lopez Esnaurrizar

" SOMETIME AGO I delivered a lecture on this subject before The Mexican Academy of Surgery, as for many years I have been convinced that splanchnic block will releive the pain due to various abdominal colics, cancer of various abdominal organs, peptic ulcer, &c.

" I have also recently, with the encouragement of my South American colleagues, embodied my observations and published them in a book entitled *Dolores Mortales.*

" I was so imbued with the efficacy of this treatment that I determined to visit England to give the results of this procedure to the College of Surgeons in the hope that the method might be more widely known and tried.

" Although the method has been adopted by many surgeons in South America, I will relate only my own personal experiences."

## General Considerations

" A recognised method of studying the function of any organ is to interfere with, and, if possible destroy, the nerve supply. Any resulting abnormality can then be noted.

" This can be done, at any rate temporarily, for as long as eight weeks —and, occasionally permanently—by carrying out a paravertebral splanchnic block, with novocaine-alcohol,* on each side.

*The lecturer did not state the composition of this solution.

" I have repeatedly convinced myself and demonstrated to others that pain impulses are conducted along the splanchnic nerves, from the thoracic and abdominal organs. Such pain is immediately relieved when these nerves are blocked, e.g., the pain due to peptic ulcer.

" Leriche and Dogliotti claim to have temporarily relieved the symptoms of diabetes mellitus by this procedure.

" It is a well-known fact that the pain of varicose ulcers and also that due to endarteritis in the lower extremities is relieved by the vasodilatation produced by sympathectomy. It occurred to me that perhaps the function of abdominal organs such as the pancreas, intestine, kidney, &c., might be improved by the vascular dilatation produced by splanchnic block.

" I believe that splanchnic block will relax any muscular spasm in the digestive, alimentary, biliary and urinary tracts, and also in the coronary arteries.

" It is a common experience for all clinicians to see patients who complain of severe epigastric pain, but in whom no signs indicative of the organ affected can be elicited.

" These cases must be regarded as being due to somatic disease.

" Such a case, which was completely relieved by splanchnic block, was the first which aroused my interest in this method of treatment. It is recorded in full in *Dolores Mortales*. Since then I have had many similar cases treated successfully."

The lecturer then gave details of the various clinical conditions for which he had used splanchnic block with success. He pointed out the necessity of keeping all cases under observation as the relief might only be temporary.

Some of the cases had been diagnosed by the lecturer as acute pancreatitis. He reported that the exquisite pain in these cases had been completely controlled, the subsequent history being such that he thought the function of the pancreas had been improved by the vascular dilatation. He maintained that cases of peptic ulcer had been enabled to continue at their occupation, whereas by any other method they would have had to give up their work or seek relief by surgical interference.

Details were given of cases of diabetes mellitus treated by this method. The glycosuria disappeared and the blood sugar became normal. "Though relapses may follow dietary indiscretions, these can be corrected by a further splanchnic block."

The pain due to inoperable cancer is likewise relieved, and the patient has a painless termination to the disease.

He has used this method of treatment extensively for hypertension, but in this disease it must be repeated, as symptoms reappear usually at intervals of approximately two months.

He has even known cases of the most obstinate constipation, on which the usual purgatives had very little effect, relieved by regular injections of novocaine-alcohol into the paravertebral tissues.

Cases of renal colic and hydronephrosis in which no calculus is present are benefited by this treatment in a marked degree.

### Technique

" The injections are given in the prone position. The usual dose is 10 cc. given into each side

" Admission to hospital for a few days is desirable as a severe neuritis may develop due to involvement of the posterior nerve roots. If the patient complains of pain in the lower limbs during the injection, then it must be stopped. Any local neuralgia which results from the treatment can be relieved by diathermy.

" The treatment is more effective in the obese than the thin."

### Summary

" A series of cases of abdominal pain treated by splanchnic block has been recorded. They are too few in number from which to draw definite conclusions."

## MONTHLY DINNERS

Monthly dinners are held in the College on the second Wednesday of each month. The following are entitled to attend with their guests: All Diplomates and students of the College, and Members of the Associations linked to the College through the Joint Secretariat. It is not necessarily intended that guests should be members of the medical profession.

The dinners will be at 7 p.m. on the following Wednesdays: April 6, May 11, June 8, and July 13, 1949. There is an inclusive charge of £1 5s. (including drinks), which must be sent with the application to the Assistant Secretary at least a week before the date of the dinner. The dress is Lounge Suit or Uniform.

## DIARY FOR MARCH (15th-31st)

| | | | |
|---|---|---|---|
| Tues. | 15 | 5.00 | Mr. J. P. Reidy—Cleft Lip and Palate Repair. |
| | | 5.00 | Mr. B. W. Fickling—The Approach to Oral Surgical Diagnosis. |
| | | 6.15 | Prof. M. A. Rushton—Endocrine Effects on Teeth and Jaws. |
| Wed. | 16 | 5.00 | Mr. A. D. Marston—Joseph Clover Lecture—Joseph Clover, His Life and Achievements.* |
| Thur. | 17 | | First Membership Examination begins. |
| | | 5.00 | Mr. D. N. Matthews—Congenital Lesions of Skin and Subcutaneous Tissues. |
| | | 5.00 | Prof. Pomfret Kilner—Facial Repair. |
| | | 6.15 | Prof. M. A. Rushton—Hyperplastic Jaw Lesions. |
| Fri. | 18 | | L.D.S. Examination (General and Special Anatomy and Physiology) begins. |
| | | 5.00 | Mr. M. Oldfield—Fractures of the Facial Skeleton. |
| | | 5.00 | Mr. E. S. Lee—Cancer of the Mouth. |
| | | 6.15 | Mr. G. G. Exner—Methods for Facilitating the Extraction of Teeth. |
| Mon. | 21 | 5.00 | Dr. F. S. Gorrill—Arnott Demonstration—The Anatomy and Physiology of Bone—Part I* |
| | | 5.00 | Mr. F. T. Moore—Hand Deformities: Reparative Surgery. |
| Tues. | 22 | | Last day for applications for Annual Examinerships. |

*Not part of courses.

| | | | |
|---|---|---|---|
| Tues. | 22 | 3.45 | PROF. W. E. GYE—Imperial Cancer Research Fund Lecture—The Propagation of Mouse Tumours by Means of Dried Tissue.* |
| | | 5.00 | MR. E. W. PEET—External Genitalia: Treatment of Congenital Deformities. |
| Wed. | 23 | 5.00 | DR. FRANK ADAIR—Moynihan Lecture—The Results of Surgery in the Treatment of Breast Cancer.* |
| | | 5.00 | MR. O. T. MANSFIELD—Hand Injuries (including burns): Early Treatment. |
| Thur. | 24 | 5.00 | MR. K. BOWES—Arris and Gale Lecture—Infra-Red Photographic Studies of the Superficial Veins in the Female and their Clinical Application.* |
| Fri. | 25 | 5.00 | PROF. W. S. C. COPEMAN—Hunterian Lecture—Pathological Anatomy of Certain Forms of Lumbar Fibrositis and the role of Surgery in its Treatment.* |
| Mon. | 28 | | Demonstrations on Anatomy, Applied Physiology and Pathology begin. |
| | | 3.45 | MR. R. J. LAST—Arnott Demonstration—The Knee Joint.* |
| | | 5.00 | MR. D. BAND—Neurological Disorders of the Urinary Bladder. |
| Tues. | 29 | | Date of Council Election announced. |
| | | 10.00 | MR. A. D. MARSTON—History of Anæsthesia. |
| | | 11.15 | MR. A. D. MARSTON—History of Anæsthesia. |
| | | 5.00 | DR. B. L. S. MURTAGH—Avoidable Accidents. |
| | | 5.00 | PROF. A. FRANCESCHETTI—Cataract Associated with Lesions of the Skin.* |
| | | 6.15 | PROF. G. B. BIETTI—Protein and Animo-acid Deficiencies in Ophthalmology.* |
| Wed. | 30 | 10.00 | DR. H. G. EPSTEIN—Physics in Anæsthesia. |
| | | 11.15 | DR. H. G. EPSTEIN—Physics in Anæsthesia. |
| | | 5.00 | DR. G. EDWARDS—Pre-operative Medication. |
| | | 5.00 | DR. E. HARTMANN—Psychosomatic Symptoms in Ophthalmology.* |
| | | 6.15 | PROF. H. J. M. WEVE—Ophthalmic Manifestations of Besnier-Boeck's Disease.* |
| Thur. | 31 | 10.00 | DR. E. A. PASK—Respiratory Depression. |
| | | 11.15 | DR. E. A. PASK—Circulatory Depression and Shock. |
| | | 5.00 | DR. E. A. PASK—Circulatory Depression and Shock. |
| | | 5.00 | PROF. C. GRAY—Hunterian Lecture—Surgical Treatment of the Painful Hip Joint.* |

## DIARY FOR APRIL

| | | | |
|---|---|---|---|
| Fri. | 1 | | Primary F.D.S. Examination begins. |
| | | 5.00 | Mr. GUY BLACKBURN—Erasmus Wilson Demonstration—Diseases of the Thyroid Gland.* |
| | | 10.00 | DR. E. A. PASK—Circulatory Depression and Shock. |
| | | 11.15 | DR. H. L. MARRIOTT—Saline, Plasma, and Blood. |
| | | 5.00 | DR. H. L. MARRIOTT—Saline, Plasma, and Blood. |
| Mon. | 4 | 10.00 | PROF. W. R. SPURRELL—Carbon Dioxide and Breathing. |
| | | 11.15 | DR. O. P. DINNICK—Local Analgesia. |
| | | 5.00 | DR. O. P. DINNICK—Local Analgesia. |
| | | 5.00 | MR. T. MILLIN—Surgery of the Prostate. |
| | | 6.15 | MR. T. T. STAMM—Ankle Fractures. |
| Tues. | 5 | | Final Membership Examination begins. |
| | | 10.00 | DR. C. A. KEELE—Analgesic Drugs. |
| | | 11.15 | DR. C. A. KEELE—Analgesic Drugs. |
| | | 5.00 | DR. J. K. HASLER—Spinal Analgesia. |
| | | 5.00 | MR. E. G. SLESINGER—The Surgery of Thyrotoxicosis. |
| | | 6.15 | PROF. H. J. SEDDON—Tendon and Muscle Transplantations. |
| Wed. | 6 | 10.00 | DR. S. ROWBOTHAM—Continuous Spinal Analgesia. |
| | | 11.15 | DR. A. H. GALLEY—Caudal Analgesia. |
| | | 5.00 | DR. M. DAWKINS—Epidural and Posterior Splanchnic Block. |
| | | 5.00 | SIR ARCHIBALD MCINDOE—Fundamentals in Plastic Surgery. |
| | | 6.15 | MR. H. A. BRITTAIN—Operative Treatment of Tuberculous Disease of Larger Joints. |
| | | 7.00 | Monthly Dinner for Fellows, Members and Licentiates (see page 194) |

*Not part of courses.

| | | | |
|---|---|---|---|
| Thur. | 7 | | Final F.D.S. Examination begins. |
| | | 10.00 | DR. W. S. MCCONNELL—Nitrous Oxide and Dental Anæsthesia. |
| | | 11.15 | DR. BERNARD JOHNSON—The Analeptic Drugs. |
| | | 5.00 | DR. W. D. WYLIE—Cyclopropane and Absorption Technique. |
| | | 5.00 | PROF. A. M. BOYD—Vascular Surgery. |
| | | 6.15 | Mr. B. H. BURNS—Open Fixation in Fractures of the Shafts of the Long Bones. |
| Fri. | 8 | | D.M.R.D. Examination (Part I) and D.M.R.T. Examination (Part I) begin. |
| | | | Date of Faculty of Dental Surgery Board Election announced. |
| | | 10.00 | DR. W. D. WYLIE—Cyclopropane and Absorption Technique. |
| | | 11.15 | DR. T. CECIL GRAY—Curare and like substances. |
| | | 5.00 | DR. T. CECIL GRAY—Curare and like substances. |
| | | 5.00 | Mr. R. J. MCNEILL LOVE—Surgery of the Biliary System. |
| | | 6.15 | PROF. G. PERKINS—Manipulation of Joints. |
| Mon. | 11 | 10.00 | DR. R. JARMAN—Intravenous Anæsthesia. |
| | | 11.15 | PROF. R. R. MACINTOSH—Ether and Ethyl Chloride. |
| | | 5.00 | PROF. R. R. MACINTOSH—Chloroform and Trichlorethylene. |
| | | 5.00 | DR. J. CRAFT—Amputations, Limb Fitting and Artificial Limbs. |
| | | 6.15 | SIR HARRY PLATT—Cystic Lesions of Bone. |
| Tues. | 12 | 10.00 | DR. I. W. MAGILL—Intubation. |
| | | 11.15 | DR. A. PARRY BROWN—Anæsthesia for Thoracic Surgery. |
| | | 5.00 | DR. A. PARRY BROWN—Anæsthesia for Thoracic Surgery. |
| | | 5.00 | PROF. LAMBERT ROGERS—Tumours of the Pituitary. |
| | | 6.15 | MR. JOHN FOSTER—Plastic Surgery of the Eyelids. |
| Wed. | 13 | | D.M.R.D. Examination (Part II) and D.M.R.T. Examination (Part II) begin. |
| | | 10.00 | DR. E. H. RINK—Anæsthesia for Cardiac Surgery. |
| | | 11.15 | DR. F. T. EVANS—Anæsthesia for Perineal Surgery. |
| | | 5.00 | DR. JOHN HEWER—Anæsthesia for Neurosurgery. |
| | | 5.00 | MR. WILLIAM GISSANE—Surgery of the Hand. |
| | | 6.15 | MR. EUGENE WOLFF—Origin of the Malignant Melanomata. |
| Tues. | 19 | | Last day for nomination of candidates for the Council. |
| | | 5.00 | MR. T. TWISTINGTON HIGGINS—Abdominal Surgery in Children. |
| | | 6.15 | SIR. HUGH CAIRNS—General Principles in Intracranial Operations. |
| Wed. | 20 | 10.00 | DR. R. W. COPE—Anæsthesia for Children. |
| | | 11.15 | DR. VICTOR GOLDMAN—Vinesthene. |
| | | 5.00 | DR. VERNON F. HALL—Anæsthesia and Analgesia in Obstetrics. |
| | | 5.00 | MR. J. B. OLDHAM—Surgery of Sacrococcygeal Region. |
| | | 6.15 | Mr. G. F. ROWBOTHAM—Head Injuries. |
| Thur. | 21 | 10.00 | DR. VERNON F. HALL—Anæsthesia and Analgesia in Obstetrics. |
| | | 11.15 | DR. PHILIP J. HELLIWELL—Refrigeration and Electronarcosis. |
| | | 5.00 | DR. STANLEY ROWBOTHAM—The Relation of Endocrine Imbalance to Anæsthesia. |
| | | 5.00 | MR. J. E. A. O'CONNELL—Surgical Treatment of Neuralgias. |
| | | 6.15 | SIR GORDON GORDON-TAYLOR—Some Aspects of Cancer Surgery. |
| Fri. | 22 | | D. Phys. Med. Examination (Part I) begins. |
| | | 10.00 | DR. RONALD WOOLMER—Convulsions. |
| | | 11.15 | DR. RONALD WOOLMER—Oxygen Therapy. |
| | | 5.00 | Dr. W. D. WYLIE—Pulmonary Complications. |
| | | 5.00 | MR. E. W. RICHES—Surgery of Urinary Calculi. |
| | | 6.15 | MR. RONALD MACBETH—Osteomyelitis of the Skull Bones Secondary to Sinusitis. |
| Mon. | 25 | | Lectures on Basic Sciences begin. |
| Tues. | 26 | | Last day for applications for Lectureships. |
| Thur. | 28 | 5.00 | PROF. C. F. M. SAINT—Stomatodocal Ruminations Clinical and Non-Clinical.* |
| Fri. | 29 | | Voting papers for Council Election issued. |
| | | | L.D.S. Examination (Properties of Dental Mechanics and Dental Materials) and D. Phys. Med. Examination (Part II) begin. |
| | | | Last day for nomination of Candidates for Faculty of Dental Surgery Board. |
| | | 5.00 | PROF. R. I. HARRIS—Moynihan Lecture—Spondylolisthesis.* |

*Not part of courses.

# THE SURGICAL TREATMENT OF CARCINOMA OF THE PANCREATODUODENAL AREA

Lecture delivered at the Royal College of Surgeons of England

on

8th July, 1948

by

Richard B. Cattell, M.D.

Department of Surgery, Lahey Clinic, Boston, Massachusetts

DURING THE LAST 15 years considerable progress has been made in the treatment of malignant disease. In the field of general surgery three lesions have been successfully attacked which were previously considered to be hopeless and inevitably lethal. Carcinoma of the œsophagus can now be resected with restoration of continuity of the gastrointestinal tract; carcinoma of the lung may have a chance for cure by lobectomy or pneumonectomy; and an appreciable number of carcinomas of the pancreas may be removed with some hope of permanent relief.

The fundamental principles required for a successful operation for malignancy have long been established, but it was necessary to have other advances as an adjuvant before recovery could be anticipated after the extensive operative procedure which was required for carcinoma of the pancreas. Improvements in anæsthesia, better understanding of the physiology of the pancreas and liver, realisation of the importance of high protein and carbohydrate and low fat diet, supplemental vitamin therapy (particularly vitamin K), ability to combat surgical shock, as well as an increasing surgical experience, have all aided in permitting a successful outcome.

The advances which have been made in the surgical treatment of cancer of the pancreas are the result of the efforts of many surgeons on the Continent, and in England, Canada and the United States. No individual surgeon has had sufficient experience to work out all the complicated problems involved, and in order to evaluate properly the present status of this major surgical problem it is necessary to pool the experiences of all to determine what has been accomplished.

It is for this reason that I wish to report our work at the Lahey Clinic, so that it can be reviewed critically. There are many surgeons of great experience who feel that operations for cancer of the pancreas offer no chance for cure. In this communication I wish to present a series of 56 pancreatoduodenal resections and to describe a new palliative

procedure used in certain cases which are definitely inoperable. I reported this operation last year, and have now performed it on 23 patients.

## LITERATURE

Excellent reviews of the literature dealing with the surgical treatmen of cancer of the pancreas have been made by Gordon-Taylor, by Whipple and by Hunt, to which reference can be made. Most of the early reports dealt with local excision of lesions involving the ampulla of Vater. Gordon-Taylor reported (in 1934) the removal of a carcinoma of the body of the pancreas performed in 1927, with the patient surviving in good health for a period of seven years. Prior to this only two successful resections of malignant tumours of the body by subtotal pancreatic resection had been reported by Serafini and Grekoff. However, William Mayo and Roscoe Graham had done local resections for malignant tumours of the body in the form of hyperfunctioning malignant adenomas of the islet cells.

All efforts to remove carcinomas of the head of the pancreas by radical operation had failed, which led Gordon-Taylor to state in 1934: "Time may demonstrate that a more extended operation in the form of duodeno-pancreatectomy improves the end-results of those cases which are still operable when they come to laparotomy; the technique of this operation has hardly passed the experimental stage."

It remained for Whipple to bring Gordon-Taylor's prediction to fruition, for in the following year (1935) he and his associates reported the first successful pancreatoduodenal resection, which was performed in two stages without anastomosis of the pancreatic duct. A few months later in the same year Hunt reported a similar operation with anastomosis of the duct of Wirsung. Trimble in 1941 described a successful one-stage operation. Due to the interest created by Whipple's experiences, described in his original and subsequent reports, over 300 resections were performed in the next 10 years by Hunt, Orr, Harvey and Oughterson, Brunschwig, Waugh, the author, and others.

## DIAGNOSIS

Carcinoma of the pancreas is fortunately not a frequently encountered lesion, representing only 1 per cent. of malignant lesions. The head of the pancreas is most often involved (Ewing). In less than 7 per cent. is the lesion confined to the tail or body. This is fortunate, since rarely will a tumour in this area be discovered in an operable stage because of the paucity of symptoms. If one includes all malignant lesions in the pancreatoduodenal area—carcinoma of the common duct, ampulla of Vater and duodenum as well—the total incidence approaches 2 per cent. It is fortunate that lesions of greater frequency occur in the head of the pancreas, which may produce early symptoms because of obstruction of the biliary tract or duct of Wirsung. Cancer of the pancreas occurs twice as frequently in women, and 70 per cent. are found between the ages of 50 and 70 years. In the past five years we have encountered the lesion in 165 patients.

The diagnosis of carcinoma of the pancreas is one of the most difficult in medicine in the absence of obstructive jaundice, and it is for this reason that so many patients are operated upon at a stage when resection can no longer be done. In a clinical review of our cases, Kiefer found that 38 per cent. did not have jaundice when first seen. In the absence of jaundice, epigastric pressure, discomfort or pain is most frequently present. This is usually on the right side, with radiation across the median line. At times the sole symptom will be high lumbar boring back pain, only relieved by a sitting position aided by leaning forward. Anorexia with resultant weight-loss is the next most common symptom, usually amounting to 20-50 lbs. Indigestion, nausea, vomiting, diarrhœa or constipation may be present, but are not more characteristic of this lesion than of other gastrointestinal disturbances. Melena and fever are less frequently seen.

The characteristic story of a patient with carcinoma of the ampulla or head of the pancreas is one of gradually progressive obstructive jaundice with associated gastrointestinal symptoms, weight-loss and anæmia, with or without pain. The presence or absence of the latter is of little help in ruling out malignancy. After a review of 105 patients who had been operated upon, we were able to get a clearer picture of the symptoms produced by lesions in different locations. From this experience it now seems possible to differentiate before operation, lesions in the pancreas and those in the ampulla of Vater. If jaundice is the first symptom, the lesion should be found in the common duct or ampulla; but if digestive or bowel symptoms, together with weight-loss and pain occur first, with jaundice later, the lesion is in the head of the pancreas. This is the result of early block of the pancreatic ducts, decreasing or excluding the pancreatic ferments from the duodenum.

There are few significant physical findings exclusive of icterus. In only 26 per cent. of our patients was there thought to be a palpable mass. Evidence of weight-loss is usually obvious. An important finding is hepatic enlargement, which is proportional to the duration of the jaundice. If in addition there is a palpable gall-bladder, this should establish the diagnosis. The gall-bladder, even when dilated, may be difficult to palpate because of displacement by the liver, and is usually found as far lateral as the anterior axillary line. Indeed, the use of Courvoisier's law of a distended gall-bladder with associated hepatomegaly will generally establish the diagnosis.

Laboratory tests are of little aid in establishing the diagnosis. Serum amylase values are normal, although the lipase and alkaline phosphatase values may be moderately elevated. Diagnostic biliary drainage will usually be negative, but may show absence of bile and the presence of blood. Malignant cells are not recovered, and no positive Papanicolou smears have been reported. There may be some disturbance of the glucose tolerance test.

Likewise, roentgen studies will generally be negative during an operable stage. An irregular mucosal pattern of the second portion of the duodenum may be observed, or there may be an increased distance between the first and third portions of the duodenum; but this implies a large tumour.

The diagnosis of carcinoma of the ampulla or head of the pancreas will usually be made in the presence of painless obstructive jaundice with hepatic enlargement and a palpable gall-bladder. Carcinoma of the body of the pancreas will be suspected in the patient with vague digestive symptoms and epigastric or back pain, in whom other more common lesions have been excluded by thorough studies. It can be confirmed only by an exploratory operation. The diagnosis is thus one of exclusion, and operation should be advised as early as possible. Fortunately, all patients who are considered to have obstructive jaundice, after appropriate liver function studies, should be explored, at which time the diagnosis can be confirmed.

## PRE-OPERATIVE PREPARATION

A careful evaluation of each patient's condition is essential, as many of them are of advanced age and are in a very debilitated condition, representing poor surgical risks. The utilization of liver function tests—cephalin flocculation, thymol flocculation and thymol turbidity, estimation of the prothrombin synthesis—is important, not only in establishing the diagnosis, but in determining the condition of the patient. The bromsulphalein test should not be used, as retention is always high. Repeated determinations of the icterus index and bilirubin will indicate whether the condition is progressive. Blood cell counts and serum protein values guide in the pre-operative preparation. Anæmia must be corrected by whole blood transfusions; serum protein may be raised by parenteral administration of amino acids as well as blood, but pooled plasma should be avoided. High protein, high carbohydrate, low fat diet is given, and is more effective in elevating the serum proteins than protein given by parenteral means. Vitamin concentrates of vitamin B complex and vitamin C are useful, and all patients should receive vitamin K subcutaneously two or three times daily, irrespective of the prothrombin level. Electrolyte balance and fluid requirements are met by daily intravenous medication with adequate glucose to aid liver function. If a patient is deeply jaundiced, operation should be delayed for only a few days, since a first-stage operation can accomplish much more in a short time than medical treatment over two or three weeks.

## ANÆSTHESIA

In view of the technical difficulties encountered in performing pancreatoduodenal resection, it is very important to have an anæsthetic which provides the maximum of relaxation and contracted intestines; but it must be selected on the basis of safety. At the Lahey Clinic we prefer fractional or continuous spinal anæsthesia, utilizing pontocaine

weighted with glucose. It is supplemented by pentothal intravenously, and a light gas-oxygen general anæsthetic of ethylene or cyclopropane. We have also used a general anæsthetic and obtained relaxation with curare. Unless good operating conditions are present, the technical hazards of the operation are increased beyond reason. Continuous intravenous administration is maintained, and two blood transfusions are given during the procedure. Patients may be kept in good condition throughout the operation of 2½ to 5 hours by these means if hæmorrhage is avoided.

## OPERATION

Operation for carcinoma of the tail or body of the pancreas offers little difficulty except in relation to the extent of the process. There are few vital structures to be protected, mainly the inferior and superior mesenteric vessels. The procedure is facilitated by removal of the spleen, thus making easy the dissection of the tail and body after ligation of the superior and inferior pancreatic vessels. In view of the few cases of cancer in this area being suitable for resection, I wish to limit the discussion of operation to carcinoma in the region of the head of the pancreas.

The most essential feature of an operation for carcinoma in the pancreatoduodenal area is a block excision which includes the pyloric end of the stomach, all of the duodenum and the first part of the jejunum, the lower end of the common duct, and the head and part of the body of the pancreas. This includes the nodes found to the right of the duodenum and those in the lower gastrohepatic omentum and suprapancreatic area. In the performance of this procedure the gastrointestinal and biliary tracts and the pancreas are interrupted. Restoration of the gastrointestinal tract can be accomplished by end-to-end or end-to-side gastrojejunostomy. The biliary tract is anastomosed by joining the gall-bladder to the jejunum in the two-stage operation, and the common duct to the jejunum in the one-stage operation.

It is my opinion that many of the post-operative complications and deaths have been related to pancreatic fistula, and earlier I called attention to the importance of anastomosis of the duct of Wirsung to the jejunum in all patients having pancreatoduodenal resection. This can be accomplished by a closed method, utilizing a pressure necrosing suture if the duct is small, or an open anastomosis over a tube if the duct is dilated.

We have anastomosed the duct in 55 patients, with one failure of the anastomosis to hold. The incidence of pancreatic fistula can be decreased by this means.

## CONTRA-INDICATIONS TO RESECTION

As one's experience increases, it becomes evident from the results that resection for advanced malignant disease in this area is not worth while. If the line of resection passes through an area involved by the process, it is quite probable that death will be hastened by spreading the malignancy throughout the peritoneal cavity.

I have previously presented four contra-indications to resection as follows: (1) distant metastases; (2) local spread with direct invasion beyond a possible limit of resection; (3) involvement of the superior mesenteric vessels; and (4) involvement of the portal vein. Fortunately, one can by proper exploration and dissection determine whether these findings are present before becoming committed to resection. Unless there be careful selection of cases suitable for resection, the operation will have a high mortality, and it will be ill-favoured by most general surgeons. I confess to performing a number of resections in the past, which I feel now, in the light of further experience, should not have been resected.

## CONFIRMATION OF THE DIAGNOSIS

In early cases of carcinoma of the head of the pancreas it may be impossible to feel a tumour, and biopsy is of no value. Under these circumstances the diagnosis must be confirmed by indirect evidence. These tumours arise in the pancreatic ducts and cause dilatation of the ducts, and the duct of Wirsung can be readily palpated. It is felt in the body as a "ditch" or depression that runs longitudinally. It can usually be localized, even before division of the gastrohepatic omentum, and its presence confirmed by needle aspiration. Lesions involving the ampulla of Vater cause dilatation of the biliary tract. They can be palpated with ease through the duodenal wall and a biopsy specimen may be obtained if further confirmatory evidence is desired. Biopsy of regional lymph nodes and biopsy of the liver may be helpful. In view of the fact that most of our resections have been performed without confirmatory histologic evidence, *I must emphasise that in a doubtful case either dilatation of the biliary tract or pancreatic ducts must be present to justify resection.*

## PALLIATIVE OPERATION

There is no question of the benefit derived from the relief of the obstructive jaundice. This is best accomplished by anastomosis of the gall-bladder to the jejunum. As pointed out by Dr. Lahey, diverting the bile to the stomach is less well tolerated, and an anastomosis to the duodenum might become obstructed by the malignant process. We prefer cholecystjejunostomy with a side-tracking enteroenterostomy. Unfortunately, relief of the biliary obstruction does not ameliorate the gastrointestinal symptoms or epigastric pressure and pain.

In an attempt to aid these patients further, I have recommended that the duct of Wirsung be anastomosed to the same loop of jejunum utilized for the biliary anastomosis. I have now done this in 23 patients with one post-operative death, and have been encouraged to observe that further benefit has resulted in some of the patients by this restoration of the pancreatic ferments to the gastrointestinal tract, as evidenced by gain in weight, decreased discomfort, and lessening of the digestive and bowel symptoms. I cannot yet state whether it has influenced time

of survival, and to my knowledge, it has not yet been tried by other surgeons.

A few patients have obstruction of the duodenum and require gastro-enterostomy. In a number I have also divided the gastroduodenal and inferior pancreatoduodenal arteries in an attempt to slow the rate of growth, since these vessels supply the major arterial blood supply to this area. Palliative procedures offer the maximum benefit, which is all too little, for those so unfortunate as to have lesions which cannot be resected.

## ONE-STAGE VERSUS TWO-STAGE OPERATION

There is an increasing trend for the employment of a one-stage operation for pancreatoduodenal resection. Whipple, Brunschwig and Waugh favour it. We have employed it in one-third of our cases, but do not believe it advisable in patients with long-standing obstructive jaundice. The main reason for employing it is because of technical difficulties encountered as a result of the first-stage procedure. These may be overcome by utilizing a long loop of jejunum brought over to the gall-bladder in an antecolic position at the first stage. Our own mortality is higher for the one-stage than for the two-stage procedure, even though the patients selected for the one-stage operation have been better operative risks. It is my belief that the two-stage operation should be employed in the majority of patients until a low operative mortality can be maintained.

The technique of the one-stage and two-stage pancreatoduodenal resections which we have employed has been published previously. Particular emphasis has been placed on the reconstructive part of the operation so that normal digestive, hepatic and pancreatic functions may be restored.

## MORTALITY

Due to the magnitude of the operative procedure, the poor condition of many patients, and the extent of some lesions resected, the mortality has been high, but not prohibitive. In our experience it is approximately the same as that following gastrectomy for carcinoma of the stomach 10 years ago. The reported mortality in the literature varies from 20 per cent. to over 50 per cent., and some experiences have been so disastrous that they have not been reported.

Our first patient, operated upon in 1940, had a fatal outcome after a satisfactory immediate post-operative recovery. This resulted from a persisting pancreatic fistula, causing hæmorrhage from the gastroduodenal artery. The pancreatic duct had not been transplanted. *Since that time the duct of Wirsung has been anastomosed in all cases.* Fifty-five patients have had pancreatoduodenal resection, with nine post-operative deaths, one occurring as long as six weeks after operation. Thus, in our experience over a period of eight years, 56 resections have been done

with 10 deaths—an operative mortality of 17·8 per cent. Resection was carried out in 28 per cent. of the patients, in whom an exploratory operation was performed for this condition. Some of these deaths must be considered as preventable, and were the result of doubtful judgment or technical error.

Causes of death were as follows : one from post-operative hæmorrhage, one from post-operative shock and transfusion reaction, two from peritonitis, and two with hepaticorenal syndrome. Each of the six might possibly have been prevented. One patient died of coronary insufficiency at 79 years, one of cerebral thrombosis with chronic hypertensive vascular disease, and two from uræmia. The last four make one doubt the wisdom of resection under such poor circumstances.

Twenty-three patients who were inoperable had a side-to-side anastomosis of the duct of Wirsung in continuity as well as cholecystjejunostomy. The last one on whom the operation was performed recently died after operation from hæmorrhage into the jejunum from the pancreas. Thus, this additional procedure has not added to the mortality of cholecystjejunostomy, since both procedures were done with 4·3 per cent. mortality.

## RESULTS

We should have great concern and interest in the condition of these patients after their recovery from operation. It is a pleasure to report that these patients are maintained in a good state of nutrition and health if recurrence does not occur. Forty-three per cent. of those submitted to resection live more than two years. Only two of the 46 patients surviving operation had any alteration of the blood sugar levels. Mild digestive symptoms sometimes persist, and are usually relieved by large amounts of pancreatic extract. Weight gain has been satisfactory. So far as could be determined by clinical and laboratory means, these patients are restored to a reasonably normal physiologic state. One patient is living and well six years after operation, and another five-and-a-half years. The results after resection for lesions of the ampulla are much better than those for carcinoma of the head of the pancreas. Further follow-up studies are necessary to evaluate properly what resection can accomplish for this lesion.

## SUMMARY

Experiences in the surgical treatment of carcinoma of the pancreatoduodenal area are reviewed.

In the presence of obstructive jaundice with liver enlargement and a palpable gall-bladder, the diagnosis is not difficult. In the absence of jaundice a presumptive diagnosis is made by exclusion of other lesions. Early exploration is advised.

Pancreatoduodenal resection should be limited at present to favourable lesions without demonstrable metastases or direct extension beyond the primary area.

Careful pre-operative evaluation and preparation is essential to improve liver function. The use of blood, vitamin K and a high protein diet in addition to the usual measures for preparing patients for serious operations are necessary.

In inoperable cases, benefit may be derived from anastomosis of the duct of Wirsung to the jejunum as well as from the relief of obstructive jaundice. Twenty-three operations of this type have been reported.

Resection has been carried out in 28 per cent. of the patients who had an exploratory operation. Fifty-six pancreatoduodenal resections have been carried out with 10 post-operative deaths—a mortality rate of 17·8 per cent.

Pancreatoduodenal resection can be followed by an essentially normal physiological state, with satisfactory gastrointestinal, hepatic and pancreatic function.

Over 40 per cent. of patients submitted to resection are without demonstrable recurrence for two years or more. Two patients have survived for over five years.

Additional experience is required to properly evaluate pancreatoduodenal resection for carcinoma of the head of the pancreas.

## REFERENCES


BRUNSCHWIG, A. (1943) One-stage pancreatoduodenectomy. *Surg. Gynec. Obstet.* 77, 581-584.

CATTELL, R. B. (1945) Pancreatoduodenal resection: Preliminary report of 18 cases. *New Eng. J. Med.* **232**, 521-526.

CATTELL, R. B. (1948) A technic for pancreatoduodenal resection. *Surg. Clin. N. Amer.* **28**, 761-775.

EWING, J. (1934) *Neoplastic diseases.* Ed. 3, Philadelphia, W. B. Saunders.

GORDON-TAYLOR, G. (1934) The radical surgery of cancer of the pancreas. *Ann. Surg.* **100**, 206-214.

GRAHAM, ROSCOE: quoted by Gordon-Taylor, G. (Ref. 5).

GREKOFF: quoted by Gordon-Taylor, G. (Ref. 5).

HARVEY, S. C., and OUGHTERSON, A. W. (1942) The surgery of carcinoma of the pancreas and ampullary region. *Ann. Surg.* **115**, 1066-1090.

HUNT, V. C., and BUDD, J. W. (1935) Transduodenal resection of ampulla of Vater for carcinoma of distal end of common duct, with restoration of continuity of common and pancreatic ducts with duodenum. *Surg. Gynec. Obstet.* **64**, 651-661.

HUNT, V. C. (1941) Surgical management of carcinoma of the ampulla of Vater and of the periampullary portion of duodenum. *Ann. Surg.* **114**, 570-602.

KIEFER, E. D., and MORAVEC, M. (1943) The diagnosis of carcinoma of the pancreas. *Surg. Clin. N. Amer.* **23**, 738-746.

ORR, T. G. (1945) Pancreaticoduodenectomy for carcinoma of the ampulla and ampullary region. *Surgery* **18**, 144-158.

SERAFINI: quoted by Gordon-Taylor, G. (Ref. 5).

TRIMBLE, I. R., PARSON, J. W., and SHERMAN, C. P. (1941) A one-stage operation for the cure of carcinoma of the ampulla of Vater and the head of the pancreas. *Surg. Gynec. Obstet.* **73**, 711-722.

WAUGH, J. M. (1944) Radical resection of head of pancreas and total pancreatoduodenectomy. *J. Amer. Med. Ass.* **137**, 141-144.

WHIPPLE, A. O., PARSONS, W. B., and MULLINS, C. R. (1935) Treatment of carcinoma of the ampulla of Vater. *Ann. Surg.* **102**, 763-779.

# FACIAL PAIN

Lecture delivered at the Royal College of Surgeons of England

on

1st March, 1949

by

Sir Charles Symonds, K.B.E., C.B., D.M., F.R.C.P.
Physician in charge, Department of Nervous Diseases, Guy's Hospital

BETWEEN THE MINDS of the patient complaining of pain and the doctor listening to his story there is a gulf not easily bridged. The patient's attitude of mind is severely practical. "I have a pain," he says, "and I want to be rid of it. What are you going to do about it?" For the doctor the problem is in the first place scientific. Where is the source of the pain and what is its pathology? If he can answer these questions he will know what practical steps can be taken to relieve it. This fundamental difference between the two attitudes is only too apt to develop into antagonism derived from a sense of frustration in the minds of both parties. The doctor presses his questions about the mode of onset, character and distribution of the pain, the patient in response insists on its severity and the need for relief, and is not backward in submitting his own views upon its causation. There are two ways of handling this situation—one is to let the patient tell his own story. This is well enough as prelude if it be brief. But time must be found for the second way which is to elicit by methodical questioning the essentials for diagnosis. What we must know about pain is its situation, its character, its time relationships, the factors which provoke and relieve it, its mode of onset and subsequent course, and the symptoms which may have been associated with it. Some of these questions are more simply answered for pain in the face than elsewhere. The patient can easily show with his finger where the pain is. The character of pain is a matter not easily discussed between persons who have no common experience, but fortunately for the interests of analysis there are few doctors or patients who have not had the experience of dental pain either of the aching—throbbing or sharp—neuralgic quality. Pricking or burning pains, and the tense pain of a local abscess are also experiences common to both parties. The tempo of pain is not always so clear. Some people can hardly distinguish between a pain which we should call continuous and the one which is intermittent but with a high rate of frequency. Provocation and relief are more easily described if they can be disentangled from theoretical views about causation. As for the associated symptoms, the examiner's skill and experience will count more in this part of the enquiry than in

any other. Knowing the commoner causes of facial pain he should be methodical and searching in his questions.

The scientific approach is naturally founded upon anatomy and physiology. Pain in the face must be due either to local disease or to affection of the nerve fibres conveying sensation of pain through the ramifications, branches, ganglion, root and central connections of the trigeminal nerve. I shall briefly consider these situations from periphery to centre and discuss at each level the common pathological processes involved before coming to an account of some pains in the face which are very real and distinct but have no certain pathology.

## 1. LOCAL DISEASE

Pain due to disease or injury of the superficial structures needs no comment. The teeth are richly endowed with pain fibres and are so constituted that these fibres are easily stimulated. The effect is pain of a piercing character which is usually well localised and correctly described as a toothache, but it may spread and become a pain in the face. This tendency for pain to spread beyond the boundaries of the structures supplied by the nerve stimulated is well known and attributed to irradiation within the central nervous system, where adjacent fibres are presumably excited. The referred pain usually has a dull aching quality and may persist for some time after the noxious stimulus has ceased. For example, Wolff and his collaborators found that experimental stimulation by the electric current of a carious upper pre-molar caused intense local pain during the ten minutes for which the stimulus was continued. This was followed by an aching pain along the zygoma, in the temple and for a short distance above the eye and this ache reached its maximum intensity and distribution 20 to 30 minutes after the noxious stimulation had ceased and might persist for several hours with gradually diminishing intensity. Stimulation by the same method of a lower pre-molar caused a comparable face ache which extended throughout the lower and upper jaws into the area over the zygoma and the temple to the top of the ear. Again the face ache reached its maximum intensity and distribution about 20 minutes after the toothache had ceased and persisted for some hours. The practical significance of these experiments is that facial pain from dental disease may be experienced in parts remote from the affected tooth, and at a time when no pain is felt in that tooth. Facial pain of a continuous aching type referred mainly to the areas supplied by the second and third division of the fifth nerve may therefore be due to dental disease. If so, I believe, as I was taught by my colleague Mr. Montagu Hopson, that the offending tooth can be identified by suitable tests.

There is no doubt that infection of the maxillary antrum can give rise to aching pain which may be referred to a large part of the area supplied by the second division of the fifth and also above the eye. The pain is

usually dull rather than severe, and it appears from the observations of Wolff that it is not due to increased pressure within the antrum but to the reflex congestion of the turbinates, for when they are anæsthetised or shrunken the pain is relieved. This procedure therefore is of diagnostic value.

Disease of the eye like that of the other structures we have considered may cause pain in the face, which is naturally referred to the area supplied by the first division, though it may spread to the second, the causes being corneal ulceration, iritis and glaucoma, and the pain of an aching character.

## 2. BRANCHES

Disease or injury involving the *supra-orbital* or *infra-orbital* nerves causes pain of characteristic distribution and of an aching character associated with paræsthesiæ, burning, tingling and numbness. Injury is the commonest cause, the patient usually having been involved in a car accident with a fracture of the upper or lower margins of the orbit. The history is that of local numbness immediately following the injury, the onset of pain often being delayed. These injuries are often overlooked because they are associated with symptoms of cerebral damage, and it is only when the patient has emerged from the state of traumatic confusion that he begins to complain. When he does so his complaints are sometimes regarded as neurotic, but a careful sensory examination will reveal the nature of the lesion.

I believe that there are other facial pains which may be the result of injury to the branches of the trigeminal nerve, but I shall leave these for discussion later. New growths involving the branches of the fifth nerve are another important but usually obvious source of facial pain.

## 3. THE GANGLION AND SENSORY ROOT OF THE FIFTH NERVE

These may be conveniently considered together for they are both involved in herpes, and are both liable to compression by tumours.

Post-herpetic neuralgia, which for some obscure reason is almost always limited to the first division, presents no diagnostic problems. It is usually severe and continuous and always associated with some degree of cutaneous sensory impairment. Practical experience has shown that neither ganglion injection nor root section will relieve the pain, and the probable explanation is that the inflammatory lesion is not confined to the ganglion and root but extends centrally.

Pressure upon the ganglion or its root by a tumour, aneurysm or inflammatory mass may be quite painless or cause severe pain, and I have no explanation for this variation. Tumours of the eighth nerve, for example, usually compress the sensory root but rarely cause pain, yet in a few cases paroxysmal pain like that of true trigeminal neuralgia

may be an early symptom. Pressure upon root or ganglion, however, sooner or later causes tingling and numbness, and impairment of the corneal reflex. This last sign is invaluable and should be looked for in all cases of obscure facial pain. Needless to say the functions of the other cranial nerves should also be examined.

## 4. CENTRAL LESIONS

Lesions of the descending root of the fifth nerve in the brain stem or the ascending quinto-thalamic fibres cause numbness and tingling, sometimes burning pain, but these are as a rule easily recognised.

Having reviewed those causes of facial pain which can be attributed to a known pathology I pass to others common enough, but obscure.

The first is true trigeminal neuralgia—a malady whose clinical features are so distinct that its diagnosis is easy. The pain is paroxysmal, piercing and shooting and occurs in bouts. It is referred to areas within the distribution of the fifth nerve. It begins in the second or third division and may subsequently spread to the first, but very rarely begins in the first division. In the early stages there are bouts of pain continuing for days or weeks with long intervals—it may be months—of freedom. During a bout paroxysms are usually provoked by eating, talking or contact with so-called trigger areas on the face or mucous membranes. Between the pains there is never any complaint of numbness or tingling. Examination reveals no impairment of corneal reflex or sensory loss. True trigeminal neuralgia is never due to disease of the teeth, though most patients before the diagnosis is made have had unnecessary extractions. The only remedies are alcohol injection of branches or ganglion, or section of the sensory root, which I think would be done much more often if there were enough neurosurgeons to do it.

There are certain other varieties of facial pain which are clinically well defined but of doubtful origin. One rare and striking example is supra-orbital neuralgia. The patient has daily attacks of excruciating pain in this region, continuous and lasting as a rule for an hour or two. Usually there is only one attack in the 24 hours, and at the same time day after day. Often this is the latter half of the morning, but it may wake the patient at night. Thus he continues for three or four weeks and is then completely free for months or years.

Another variety of facial neuralgia is that in which the pain is referred to the back of the eye and to the infra-orbital region and occurs in attacks which last for several hours. The pain is continuous and often described as like that of an abscess. It may be associated with lacrimation, rhinorrhea and a feeling of congestion in the nose. Sometimes there is redness and swelling of the infra-orbital tissues. The pain may extend into the upper jaw and also into the neck and shoulder. This type of neuralgia is often associated with a personal or family history of migraine and has

therefore been designated migrainous neuralgia. The headache of migraine is caused by dilatation and stretching of arterial walls, and it is quite reasonable to suppose that this may occur in the arteries of the face. It may be that supra-orbital neuralgia is of similar causation. Both varieties may respond to injections of ergotamine tartrate. Neither should be confused with true trigeminal neuralgia if the history is properly taken.

So far my task has been easy but it must be confessed that there are many patients with facial pain whose complaints cannot be fitted into any of the pigeon holes which I have mentioned. Because they are beyond our diagnostic competence they are often dubbed functional with the implication of a psychogenic basis, and indeed many of these patients do appear to be unduly anxious and preoccupied with their symptoms, and their past history reveals them as persons of what may be called the over-sensitive type. This does not, however, exclude a physical basis for their complaints.

These atypical facial neuralgias invite discussion. My contribution to this will be of speculative and doubtful value. There is one group which I think belongs to the true trigeminal neuralgias, though its mode of onset is out of the ordinary, with dull, continuous, aching pain in upper or lower jaws and a much later addition of paroxysmal pain of the classical type. The diagnosis has to wait until paroxysmal pain develops, and alcohol injection or root section will then give relief.

There is another group in which the pain follows antral infection, often with a history of antrostomy. The pain is infra-orbital, continuous, aching and sometimes burning, and is often made worse by heat so that the sufferer cannot bear to sit near a fire. It is natural to suspect that the infra-orbital nerve may have been damaged either by infection or by trauma in the course of operation, and I suspect that this is true, though the history of numbness and tingling which one expects in a neuritis is lacking. Alcohol injection of the infra-orbital nerve does not relieve these patients, nor unfortunately does avulsion of the nerve. Their pain, though it is persistent, is seldom bad enough to warrant ganglion injection, but I have seen cases in which this has been done with satisfactory anæsthesia, but without relief.

In certain respects therefore this variety of facial pain resembles causalgia, in which following injury of a peripheral nerve, especially the median, usually associated with infection, there develops continuous burning pain, which is not relieved by section proximal to the lesion.

Similar pain within the distribution of the inferior dental may follow an injection of local anæsthetic into this nerve and the history may usually be obtained that the numbness following the injection took much longer to pass off than is usual. I suspect that in these cases the needle has actually entered the nerve sheath and that the pressure of the injection has blown its fibres apart, resulting in a traumatic neuritis. If this

suspicion is correct it is an argument for slowness and care in the manner of injection. The dental surgeon's syringe perhaps lends itself too easily to injection under high pressure. Comparable pain may follow dental extractions either in the upper or lower jaw under local or general anæsthesia. The initial story in these cases is that of a genuine toothache, the pain being excited by heat and cold. Following the extraction the pain is temporarily relieved. It then returns and the dental surgeon is often persuaded to extract neighbouring teeth still without relief. Further operations may be undertaken upon the jaw. The pain continues and is apt to spread as a dull ache into the malar region, the temple and towards the ear. Both in its character and distribution therefore the pain resembles that of a toothache though by this time there are no teeth. I have seen many of these cases and have been accustomed to call them for my own purposes dental causalgia, though this is not the appropriate term. Causalgia means burning pain, and this is not a burning pain. My reason for using the term causalgia is that I suspect the mechanism of this particular syndrome may be the same as that responsible for causalgia. Causalgia results from injury to a cutaneous nerve which for reasons which are imperfectly understood passes into a state of continuous irritation. The pain which results is of the kind normally transmitted by cutaneous nerves, burning or pricking. This kind of pain, however, cannot be obtained by stimulation of a dental nerve, and I suppose that if as a result of injury a dental nerve passed into a state of continuous irritation the pain experienced would be that of toothache. I suggest, therefore, that toothache persisting after extraction may be due to local nerve injury.

There are certain other points of resemblance between true causalgia and what I shall proceed for want of a better name to call dental causalgia. Both are susceptible to emotional fluctuation. Why this is so in true causalgia we do not know. It has been suggested that at the point of injury some abnormal communication is formed between afferent sympathetic fibres and afferent pain fibres, so that reflex sympathetic stimulation from emotion excites the afferent pathways. The other curious fact is that both true causalgia and dental causalgia may continue after the nerve has been destroyed by alcohol proximal to the presumed lesion. Whatever may be the cause of dental causalgia as I have described it, measures directed towards improving the emotional stability of the patient are more effective than local treatment or nerve injection. If the sufferer can be persuaded that the pain is due not to any remaining disease but to a sore nerve, and that it must be endured perhaps for some time with the help of aspirin and codeine it will usually disappear. If it does not the reason is that the patient is of the anxious obsessional type and needs psychiatric treatment. In these patients injection of nerves with alcohol is only too apt to make matters worse, the paræsthesiæ resulting from the injection becoming a distressing source of preoccupation.

When all this has been said it must be admitted that there are a good many patients with the complaint of facial pain whose symptoms do not fit any of the categories so far described. These are the atypical neuralgias about which I find it difficult to say anything of value. Looking through my case notes I find that of 36 patients classified as atypical neuralgia, 32 were women. Hysteria is commoner in the female sex, but I could only find evidence to support this suspicion in one, and it seemed to me that there was a physical basis for her pain though she was making the most of it for reasons of her own. The general characteristics of the pain in these cases seem to be as follows: It is aching, continuous with exacerbations, and usually widespread, extending beyond the face into the back of the head, the neck and sometimes the shoulder. It is sometimes bilateral, simultaneously or alternately. In every case, however, it had begun in some part of the face or jaw and had spread later. Teeth and sinuses had invariably come under suspicion as the cause but nothing had been found. All complained bitterly of their pain. A few had had ganglion injection, or root section, done without relief and in two of them after root section cervical sympathectomy also failed. It seems as if their pain must be of central origin, but this is not to say that it is psycho-neurotic, only that we have a great deal still to learn about the mechanism of pain in general and especially in the face. We must remember that trigeminal neuralgia, though it is undoubtedly of organic origin, has no demonstrable pathology, and that there may be other patterns of facial pain of comparable significance.

Wolff and his colleagues have made some observations on the use of analgesics which are of practical value, using experimental methods of producing pain in the head in subjects trained in the assessment of their pain on a ten-point scale. They found that acetylsalicylic acid and codeine phosphate reached their peak values in raising the threshold for pain in 60 to 90 minutes after which there was a gradual fall, the total effect lasting four to five hours. They further showed that increasing the dose of aspirin above five grains, or codeine above one grain, made no appreciable difference to the rapidity, intensity or duration of the effect. It follows therefore that doses of these drugs in the amounts mentioned repeated two-hourly are more effective for the relief of continued pain than larger doses at longer intervals.

## SAYINGS OF THE GREAT

"The feasibility of an operation is not always the best indication for its performance . . ."—*Professor Sir Henry Cohen.*

"One mark of a great man is the power of making lasting impressions upon people he meets. Another is to have handled matters during his life that the course of after events is continuously affected by what he did."—*Winston Churchill.*

# THE FIRST ANNIVERSARY OF THE FACULTY OF ANÆSTHETISTS

THE FIRST ANNUAL General Meeting of the Faculty of Anæsthetists was held in the College on March 16, with the Dean of the Faculty, Mr. A. D. Marston, in the Chair. The meeting was addressed by the President of the College, Lord Webb-Johnson, as follows :

It is my pleasant duty to welcome you to the College on the occasion of your first meeting as Members of the Faculty of Anæsthetists, and to express the hope that you will be able through the Faculty to attain the important objectives which you have at heart.

The Council hopes that all those engaged in the surgical specialties or specialties allied to surgery will feel that the College is their natural academic home. We surgeons have been accustomed so to regard it throughout our professional lives, and feel sure that you will soon develop the same feeling as we have, and have a real attachment to the College. In order to foster this feeling the Council wishes to give each of the Faculties complete academic freedom, and to make the members realise that they are not only in but of the College.

Anæsthetists are clinical physiologists working in the closest collaboration with surgeons. No longer regarding the mere rendering unconscious of a series of patients as their sole responsibility, they must be qualified to be accepted as essential members of a surgical team not only at the time of an operation, but concerned with the pre-operative preparation and the post-operative care and resuscitation of the patient.

The field covered by the Anæsthetist to-day is much wider than it has been in the past. The Anæsthetist is not only the partner of the surgeon during the operation but his valued assistant before and after. The work in the " Forward Surgical Units " in the 1914-18 war and the last war showed that when the Anæsthetist was available all day, his help was invaluable in preparing patients for operation, and in tiding them through the critical hours and days afterwards.

I do not want you to get the impression that the Faculty is in any way a rival to or competitive with the Association of Anæsthetists. The functions of the two being complementary, they must overlap to a certain extent. The essential functions of the Faculty are academic—to lay down academic standards and see that they are maintained ; to draw up syllabuses for examinations ; to arrange courses of instruction and to guide the Council of the College and the Universities with regard to standards and policy. In questions of public policy the Faculty is more detached than the Association, and can make clear that certain proposals are not compatible with high efficiency. The Faculty is not concerned like the Association in the early stages of negotiations, and can therefore exert a more powerful influence in the late stages, can give guidance to members of the profession which may either lead to acceptance of proposals or make it perfectly clear that they should not be accepted.

In the Faculty you are, as in the Association, always welcome in the College, but in the Faculty you are part of the College and have all the prestige of the College behind you. You therefore carry some responsibility for maintaining that prestige, and I have no doubt that you will not only maintain it but add to it.

# POTT'S DISEASE AND POTT'S PARAPLEGIA

Lecture delivered at the Royal College of Surgeons of England

on

7th July, 1948

by

G. R. Girdlestone, F.R.C.S.

Hon. Surgeon, Wingfield-Morris Orthopædic Hospital

SPINAL CARIES IS THE most common and most dangerous form of skeletal tuberculosis. In a recent review of 664 cases, there were 241 deaths—a mortality of 36 per cent.

We owe to Percivall Pott(1) a moving description of the disasters which happened to victims in those days. Unfortunately, some of these things still occur. Therefore, I want to use the brief time at my disposal in discussing the principal dangers in spinal tuberculosis, and how best to endeavour to avoid them; and with regard to paraplegia the indications for decompression and a comparison of the available operations. It seems better to discuss a few selected points with some freedom than to attempt an inclusive description such as can be found in a text book.(2)

In spinal tuberculosis the dangers begin with *delay or mistakes in diagnosis*. An aching back is a common complaint, spinal tuberculosis rare. It is only too easy for a busy doctor to diagnose lumbago and supply the patient with a prescription and a certificate; and it is becoming increasingly fashionable for surgeons to suppose that almost the only cause for a persistent spinal pain in a young adult is the protrusion of an intervertebral disc. Unfortunately, one of the characteristic radiographic appearances in tuberculosis of the lumbar spine is the so-called "pincement," i.e., a narrowing of the disc space so that serious mistakes can easily be made. Delay in diagnosis means the failure to recognize a deadly disease, and so failure to take prompt steps, both to help the patient fight the infection, and failure to protect his vertebral bodies from weight and movement. Even more serious is it to operate through mistaken diagnosis on a patient in the advancing phase of spinal caries; the operation may be laparotomy for pain, referred to the abdominal wall, laminotomy in search of a protruding disc, or the incision and drainage of a psoas or lumbar abscess, with the disaster of secondary infection. But my present point is not so much concerned with the ill-conceived operations as with the danger of submitting a patient with carious vertebral bodies to an anæsthetic. I have seen a number of patients in whom the result on the evolution of the spinal disease has been disastrous. This is, no doubt, because during conscious life the bodies are protected by dorsal spinal muscles, which are on guard; while under the anæsthetic not only are the muscles flaccid, but various movements of the patient are carried out, which are likely to lead to crushing of the unprotected, disorganized and heavily infected bone.

We shall need all our care and observation to avoid making these mistakes; the first thing is to remember the possibility of tuberculosis as a cause of backache, and not only in children, where other causes of backache are rare! Then we listen and look for hints of the beginning of illness, and if suspicion arises we scrutinize first-class radiograms both of the spine and the chest. It is, unfortunately, possible for a patient to have had spinal tuberculosis for several weeks before X-ray changes can be discerned, and that this may even be true in the presence of paraplegia. However, in the vast majority of cases of spinal caries up for diagnosis, radiology will disclose the presence of some destructive spinal disease. To discuss the differential diagnosis is impossible here and now. I have dealt with it elsewhere.(2) Radiology of the chest is just as essential as that of the skeletal lesion, and may be even more helpful to diagnosis. The skeletal lesion is always secondary to a primary infection of lung or gland. Since pasteurization of milk has immensely reduced alimentary infection, and lack of segregation of cases of open tuberculosis has raised the incidence of primary infection of the lungs, the value of radiography of the chest is correspondingly great. In a recent review of a series of 500 cases of skeletal tuberculosis(3) active intrathoracic lesions were revealed by X-ray in 57 per cent. Pasteurization has also raised the significance of the Mantoux test.

The other dangers to which I wish to refer are:

1. Secondary septic infection;
2. Progressive disease and severe deformity; and
3. Paraplegia.

In Table 1 you will notice that while the percentage figure of deaths due to meningitis, miliary, and generalized tuberculosis is nearly the same in the dorsal and lumbar regions (between 10 and 11), the deaths due to amyloid disease are very much more numerous in the lumbar group in accord with the frequency of pyogenic infection of psoas or lumbar abscess.

The infection of a cold abscess is in truth a terrible event. Rollier(4) once referred to it as a "death sentence." Pott, though unable to prevent it, gave a realistic account of its prolonged miseries. Only if we appreciate how prevalent a danger it is in this disease and how great a disaster, shall we learn with sufficient relief and attention that *septic infection of a cold abscess can be avoided*, and this applies even to those which have ceased to be amenable to aspiration and have to be treated surgically, even those which leak. The success of the technique, which I have fully described elsewhere(2) depends upon two main factors: first, the effective general and local treatment of the disease; secondly, the most thorough care in aseptic dressing with a special antiseptic (crystal violet and brilliant green, each 1 per cent. in 75 per cent. spirit) treatment of the surrounding skin. With the exercise of sufficient care secondary infection can be avoided, then with good general treatment and local rest, the source of debris and reactionary fluids soon dries up.

Level of Lesion in relation to certain causes of death.

| | Cases | Total Deaths | Toxaemia Tb. or sepsis | Amyloid | meningitis | Miliary or Gen. tb. |
|---|---|---|---|---|---|---|
| Cervical | 21 | 9 | 3 | 2 | | |
| Dorsal | 266 | 81 | 10 | 6 | 14 | 15 |
| Dorso-lumbar .. Lumbar .. Lumbo-sacral | 330 | 130 | 43 | 27 | 15 | 19 |
| Double lesions | 47 | 21 | 7 | 2 | 2 | |
| | 664 | 241 | 90 | | 65 | |

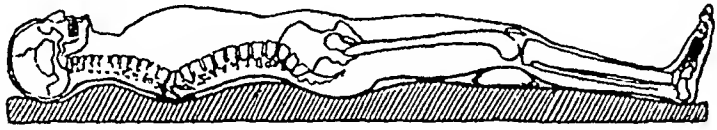
Table 1

| Level | Cases | Deaths from Toxaemia & Amyloid | Deaths from meningitis miliary generalised } tb. |
|---|---|---|---|
| Dorsal | 266 | 16 = 6 % | 29 = 10·9 % |
| Lumbar group. | 330 | 70 = 21 % | 34 = 10·3 % |

Table 2

## PROGRESSIVE DISEASE AND SEVERE DEFORMITY

The arrest of disease depends upon the healthy reaction of the patient, both general and local, and time; by a constructive reaction and the passage of time, which is much longer than many people appreciate, barriers are built up, which surround and confine the invading bacteria, then reconstruction and recalcification take place in the whole granuloma, which has replaced the disorganized tissues. To promote this general and local reaction are needed, physical rest, a good diet, open air, and all the factors which combine to make up the modern treatment of surgical tuberculosis. The lesion in particular requires rest, and that means that the softened and heavily infected bone must be protected from weight and movement, and the even greater harm of crushing weight combined with movement. All the mechanical art of the orthopædic surgeon is needed to ensure the efficacy of general and local treatment by which progressive disease and deformity is avoided. (Fig. 1.)



PAD protecting Kyphos but pressing it forward as a whole and developing Compensatory Curves just above and below

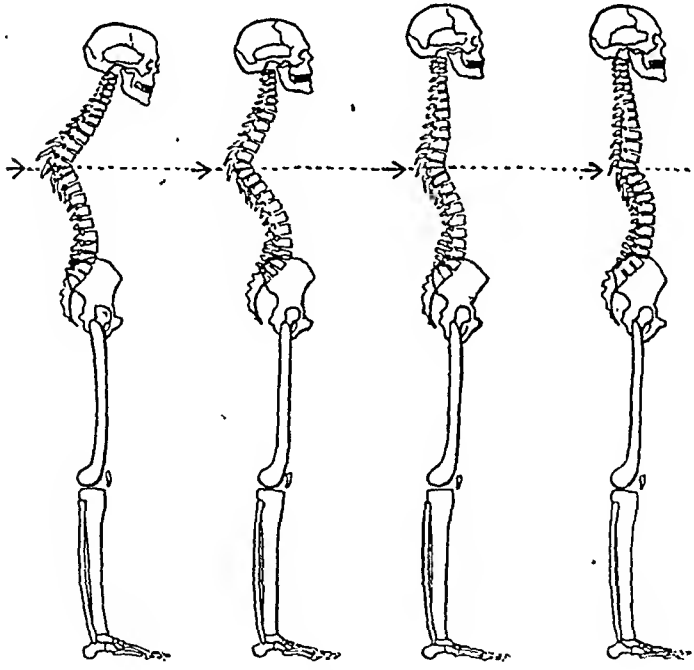
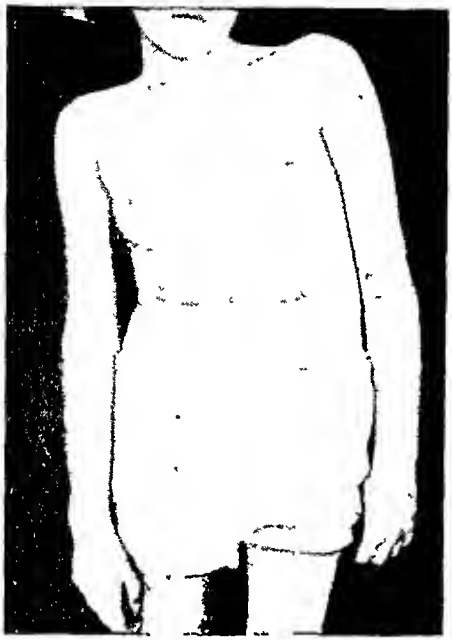


Fig. 1.

Yet these dangers are still present, especially in children, and are very liable to increase after the child is allowed up and out of hospital. (Figs. 2, 3, 4 and 5.)



Figs. 2 and 3. A case recently admitted to the Wingfield-Morris Hospital after a period at home following a long period in a Hospital for pulmonary and non-pulmonary tuberculosis. (See also Figs. 4 and 5.)

In order to avoid such occurrences treatment must be fully accurate and complete, to minimize deformity and to bring about a satisfactory degree of stability before the patient leaves hospital.

In children, sound healing can be achieved by rest and time, rest of the infected part, effective, uninterrupted and prolonged, in an open-air orthopædic hospital. Fortunately, prolonged decubitus does them little harm, providing that its dangers are recognized and avoided.(5)

When at the end of this conservative treatment some instability of the spine remains, grafting may be advisable. This happens most often in the lumbo-sacral region; for here external splintage is ineffective or very cumbersome.

The younger adults can be brought on step by step, through the preliminary stages of the disease, and grafting performed if, and as soon as, it is indicated. It is wrong to graft before the patient is thoroughly fit for the operation; and before the total extent of the foci in the vertebral bodies has had time to appear in the X-ray films, or in the hope of achieving a short cut whereby the patient can return sooner to his work. In these restless days it is well to remember the above rules, which are based on long experience, and drafted to avoid genuine and serious dangers.

Fig 4 Radiogram of the same case. Note extreme pelvic tilt. (See also Figs. 2, 3 and 5.)

Fig. 5. Radiogram of same case. Note angular deformity. (See also Figs. 2, 3 and 4.)

In the elderly the position is different. We must now abandon the principle which has guided us hitherto. We cannot await sound healing because in the elderly natural sound healing does not occur.

Not only is this so, but old people react unfavourably to prolonged rest on a frame or plaster. For the first three or four months immobilization is necessary and helpful. Their general health improves, they feel better, and their sedimentation rate begins to fall. But in spite of all this, radiograms generally fail to show any evidence of arrest of the destructive process. This is what one has learnt to expect in an active tuberculous knee in an elderly person, where amputation is often the right treatment, for it eliminates a major focus and allows the patient to get up as soon as he ceases to benefit from rest in bed. In the spine the best we can do is to carry out posterior spinal fusion without further delay, and to do the strongest and most thorough grafting possible, because it is likely that the grafts will have to share with the lateral articulations all the weight and all the strains imposed upon the spine at this level. When this operation has been done at about three months, one can generally get the patient out of bed within a total of eight or nine months; and this is what they need, *and* appreciate.

## POTT'S PARAPLEGIA

Pott's Paraplegia endangers the life of the patient and the conduction of his spinal cord. To live on at the cost of permanent damage to one's cord is poor comfort! Yet the teaching of the past, even the fairly recent past, leads in that direction, since it shows an unbalanced preference for the continuance of conservative treatment almost to the bitter end! It is even now widely regarded as "correct" to persist with conservative treatment for six months despite increasing damage to the cord, with its associated dangers and discomforts, because operative decompression has been most unfairly discredited. Too often the result is a state which Percivall Pott(1) described as "Dragging on a miserable existence, confined to a great chair, or bed, totally deprived of the power of locomotion, and useless, both to himself and others."

"This, in an infant, is most melancholy to see; in an adult, most miserable to endure."

It is high time that fresh light should be thrown on the treatment of Pott's Paraplegia! The prevalent misconception of "correct" treatment has followed the two admirable essays by Butler(6) and Seddon(7) in 1935. Unfortunately, from their statistical review of operative decompression the truth did not emerge. The relatively good results of the relatively few well chosen, well timed and well performed operations for decompression were inextricably mixed with a large number of disastrous results following operations carried out without adequate orthopædic precautions.

I have already mentioned the destructive effect that the anæsthesia associated with any operative procedure has upon the evolution of spinal

caries, because of the loss of the protection of dorsal and muscular control. Anæsthesia and operation in the presence of paraplegia is naturally even more dangerous; and decompression was condemned because of the many terrible results. Butler wrote to me in 1937:

"It astonished us, and I know it would astonish you to find how lightly laminectomy was carried out in many patients in our series (often in the presence of active disease) without really adequate care at the time, or afterwards, to preserve mechanical efficiency in the spine as a whole."

Indeed, both these authors recognize the misleading nature of the statistics they gathered from miscellaneous sources, and are in agreement as to the danger of undue delay in decompression of the spinal cord.

As an instance of the degree to which the influence of these figures is still at work, I can quote recent figures from a first-class orthopædic hospital giving a series of 118 cases of paraplegia in which decompression was carried out in only 16. My correspondent writes(8):

"It has been the policy of this hospital to treat paraplegias conservatively to a very large extent."

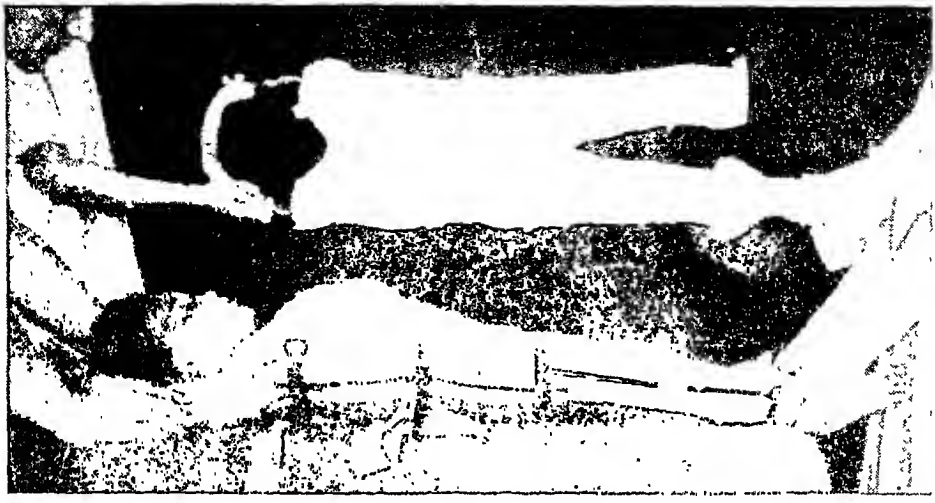
Of course it is wholly right to condemn decompression in Pott's Paraplegia unless it is done by surgeons experienced in spinal tuberculosis, and with the maintenance of effective and uninterrupted immobilization of the spine before, during and after operation. But this was made possible by the addition of a "turning case" (Figs. 6A and 6B) to the frame or plaster bed more than 30 years ago in Shropshire.

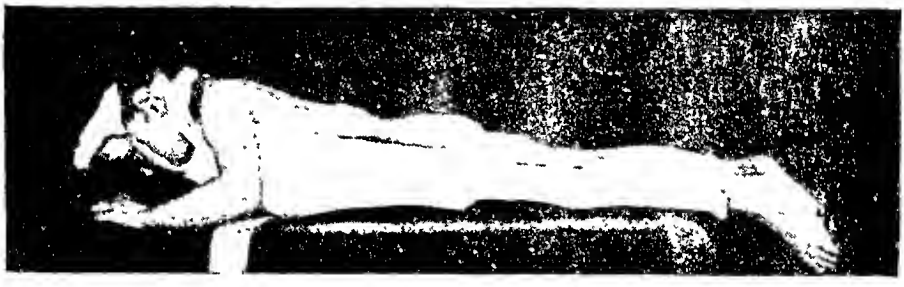
Ever since then this has been the practice of the writer and his colleagues, and has proved most satisfactory. The use of some such continuous control has been the practice in the best orthopædic centres for many years, and has altered the whole situation. One should note, however, at this point that the complete control of the spine, with the protection of the diseased vertebral bodies, depends on the integrity of the lateral articulations. The importance of this will be apparent when I discuss the lateral approach to the spinal theca.

We can, therefore, assess the indications for operative decompression by costotransversectomy or laminectomy (without facetectomy) free from fear of endangering the structural stability of the spinal column; but we are still face to face with a very serious and dangerous complication of a disease, very serious and dangerous in its own right.

## Timing of the Operation

Pott's Paraplegia very seldom appears after a patient has been for some considerable time under good general and local treatment, much more commonly before he comes into hospital or after he has gone home. So the first step is to establish full general treatment and local immobilization. When the paresis is mild, or moderate, and of recent appearance, a period of conservative treatment favours the patient's reaction to the





Figs. 6A and 6B. Turning case.

disease and allows repeated observation of the neurological signs. How long to wait is often difficult to decide, and calls for a careful balancing of the neurological and general clinical picture.

In cases in which there is evidence of severe or progressive compression it may be advisable to operate without more delay than is required for settling the patient on frame or plaster bed and providing a good turning case. In such circumstances one operates because the relief of the spinal cord appears of such urgency that it is unwise to allow time for conservative treatment to exercise a favourable effect—*qua* disease, and perhaps also *qua* paraplegia. This justifiably contravenes the golden rule that it is wrong to perform a major operation on a patient who is still subject to the active invasive stage of skeletal tuberculosis—a golden rule because such a patient is ill-fitted to stand shock, which is an immediate danger to his life and a set-back to his body's attempt to put up a successful fight against the disease. Furthermore, at this stage the body's immunity is at its weakest, and there is risk of the dissemination of tuberculosis from the escape, during or after the operation, of infected material into veins or lymphatic channels. As time passes, provided that the total response of the patient is favourable, operation carries less

and less risk, so that when the phase of successful reaction has been established the danger of dissemination is almost nil.

A decompressing operation for a mild, or even a moderate, degree of Pott's Paraplegia is not then ordinarily indicated until the patient has been for a period given the benefit of good general treatment in the open air, coupled with effective immobilization of the spine. It is true that G. L. Alexander has recently written: "The indications for decompression of the cord in Pott's disease are, we think, no different from those in cord compression from other causes."(9) But this disregards contra-indications, and I would prefer to balance the indications and contra-indications very carefully in each case, with due regard for the patient's life and an even greater regard for the restoration of the function of his spinal cord I say this because I believe that most patients would choose to run the risk of early operation if it favoured the recovery of the cord, but even more because I believe the decompression (by the skilful and gentle performance of one or other of the older operations) is likely to be of great, indeed, critical, value to the cord and do relatively little harm to the patient.

With regard to the preliminary period of conservative treatment, six months has been suggested, but I am sure that this is much too long, even in mild or moderate paraplegia, and would operate in six weeks if there were no encouraging signs of improvement. Furthermore, in severe or advancing paraplegia the time soon comes when further delay is bad, not only for the patient's spinal cord, but for his mind and body, too. All are now deteriorating. There is no excuse for further inaction.

In order to favour the management of this complex syndrome, all cases in which Pott's Paraplegia develops should be sent at once to a first-class orthopædic centre, where special nursing skill and all facilities for open-air treatment and expert immobilization exist, and where mature judgment and operative skill are always available.

## Choice of Operation

In this brief review it has not been possible to discuss pathology at any length; there has been an excellent recent review by Seddon.(10) But when the choice of operation is to be made a great deal depends upon whether the paraplegia is associated with active disease or apparently the result of long continued cumulative effects of deformity at a much later stage. I must also omit any discussion of cases in which the disease affects the posterior parts of the vertebral column.

In paraplegia associated with the active phase, often called "early" paraplegia, the compression is commonly from in front and generally associated with the dissolution of the somatic column amounting to what has often been called "pathological fracture." (Fig. 7.) This means a gap in the column through which the debris and pus resulting from the destructive processes may collect in front, to the sides, or behind the bodies, are in communication. Therefore, in cases where radiograms

Fig 7. Pathological fracture with free communication of abscess

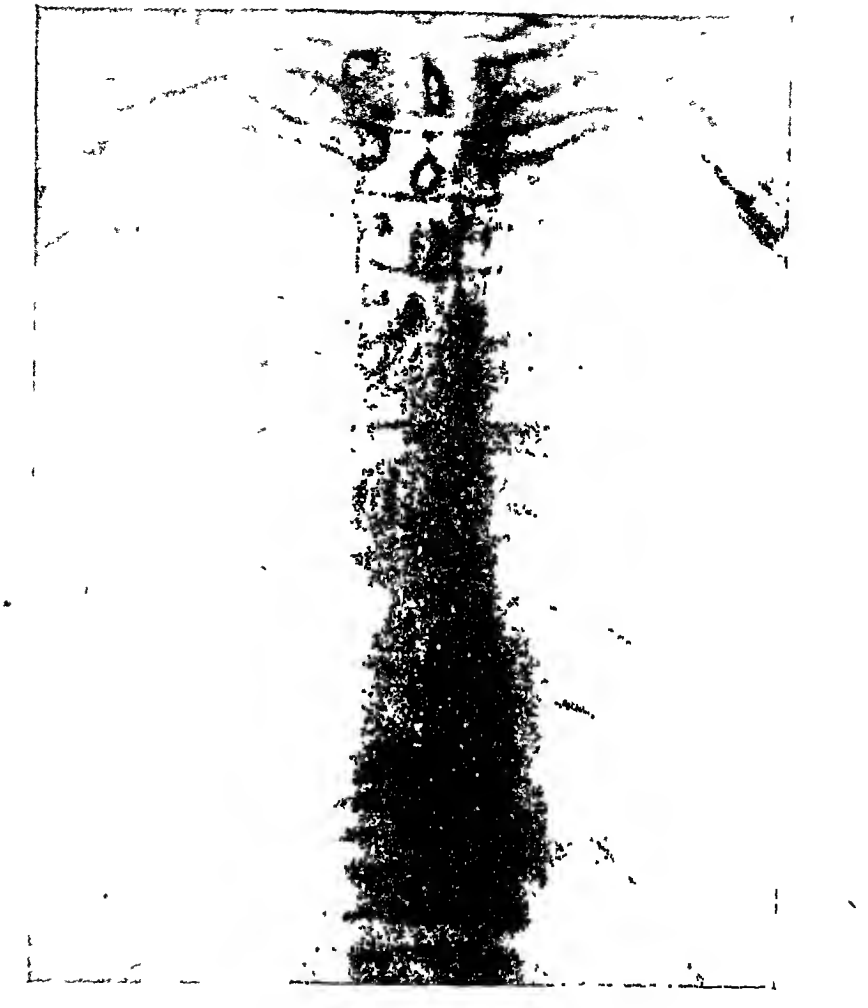


Fig. 8. Taut paravertebral abscess.

show evidence of a large taut paravertebral abscess it is obviously foolish to do a laminectomy, though I had to learn this by the process of trial and error! (Fig. 8.)

In such a case costotransversectomy with complete evacuation of the abscess will often suffice, especially where there has been time for the destructive process to become arrested as a result of general and local treatment. It may have to be repeated in preference to laminectomy on radiological evidence. It can always be followed by laminectomy and grafting through another route if, after three or four weeks, there is no evidence of relief. (Figs. 9A and 9B, 10 and 11.)

By this means decompression can be achieved without any interruption of the series of bilateral articulations which, with the control of antero-posterior splintage, protect the diseased bodies. Costotransversectomy

and laminectomy (without facetectomy) either one, or both in series, have no harmful effect on the stability of the spine under standard modern orthopædic care. This is often imperfectly understood, and laminectomy has been falsely accused, even quite lately by Alexander. Yet this fact is of fundamental importance in regard to the choice of operation for "early" paraplegia.

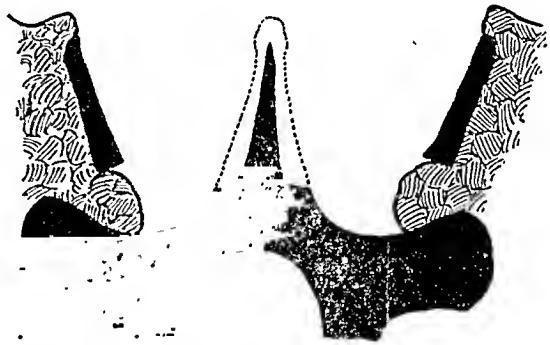


Fig. 9A. Showing motor saw cuts into a spinous process.

Fig. 9B. State of affairs after reflection of osteoperiosteal flaps in the area of the laminectomy and two vertebræ above and below.

Fig. 10. Showing grafts bridging defect left by laminectomy, with their lateral osteogenetic hosts.

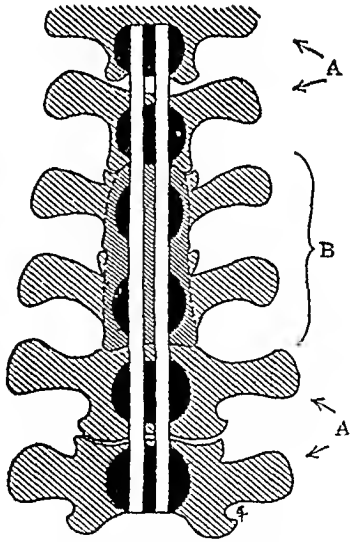
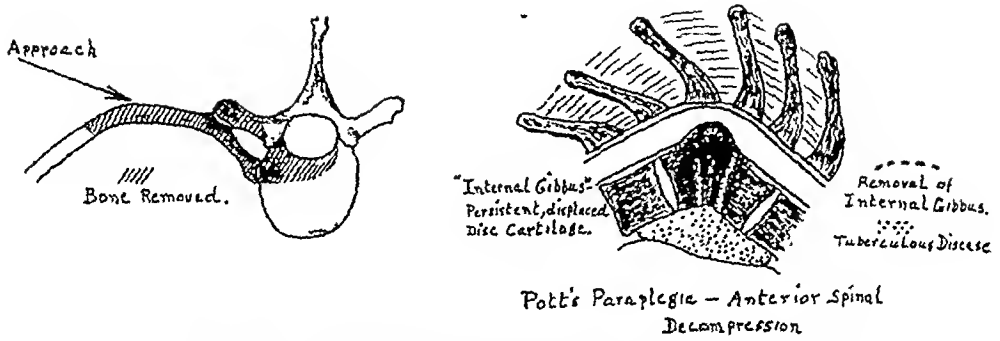



Fig. 11.

Fig. 11. Diagrammatic representation showing the grafts bridging the area of laminectomy (B) and supported on shoulders of spinous processes and laminæ of two healthy vertebræ above and two below.

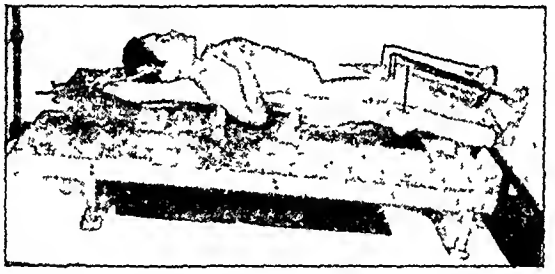
## Lateral Rhachotomy

To costotransversectomy and laminectomy there has recently been added (Capener, 1935([11])) a lateral approach. This was designed for access to the structures lying in front of the theca in a case of late paraplegia with severe angulation.




*By kind permission of The Editor,* Proceedings of the Royal Society of Medicine.

Fig. 12. Alexander's antero-lateral approach (diagrammatic).



*By kind permission of The Editor,* Proceedings of the Royal Society of Medicine.

Fig. 13. Skeletal skull traction.

Alexander(9) and Dott in Edinburgh have developed independently a rather similar antero-lateral approach. (Fig. 12.) Alexander emphasises the advantage of the exposure and complete evacuation of the paravertebral abscess after costotransversectomy on the way in, and his approach is rather more anterior than that of Capener. Both take away the pedicles, Alexander after a radical costotransversectomy, Capener keeping rather farther back and doing a partial hemi-laminectomy. I think it is probable that these two surgeons have developed their lateral approach with rather different aims. Alexander uses his approach at any stage early or late; whereas Capener developed his operation particularly for "late" paraplegia with severe angulation. If lateral rhachotomy is to be applied to active phase paraplegia, I would agree with Alexander that it is wise to include thorough evacuation of any paravertebral abscess there may be. However, I do not think that any general application of lateral rhachotomy to active-phase paraplegia is wise at present. It is true that Alexander goes out of his way to maintain immobilization during and after operation by skeletal skull traction (Fig. 13) in cervical and upper thoracic disease. But I feel that it is wrong to interrupt the integrity of the bilateral series of articulations during the active phase of caries. These fears are based upon anatomical considerations and may, perhaps, be set at rest when the end

results of an adequate series are known in, say, 10 years' time. In the meantime I strongly recommend that the operation of *lateral rhachotomy should be confined to "late" paraplegia in the presence of severe angulation* (Fig. 14) *and sound or reasonably sound all round spinal stability.*

Fig. 14. Severe angulation.

Under these circumstances an antero-lateral approach has everything to commend it, since it offers the cord which has been stretched over an

extreme angulation its two great needs, viz., both a smoother and a shorter path. Furthermore, the severity of the angulation facilitates the approach. On the other hand, during the active phase there is neither extreme angulation—to facilitate the approach—nor is there the special need for extensive lateral access for the road straightening work; nor again, and this is a vital drawback, is there any established stability to justify the structural damage. Furthermore, Somerville(8) has written: "When there is a big kyphos, the operation is technically difficult, and when there is no kyphos it is very difficult." This sentence is very significant, since in the active phase of caries the patient is hardly fit for an extensive difficult operation (which cannot be hurried), and unfit for one which is very extensive and very difficult! (Fig. 15.)

POTT'S PARAPLEGIA—Anterior Spinal Decompression.
Curved left paramedian incision around Gibbus -D4-5.
Superficial Muscles cut near spines.
Erector spinæ muscle displaced medially.
Ribs 3, 4, 5, 6 resected. Transverse Processes removed.
Anterior parts of pedicles removed, exposing Theca.
Internal Gibbus removed from vertebral bodies exposing anterior surface of Theca.
Intercostal Nerves are Guides throughout.

Fig. 15. Alexander's operation; antero-lateral approach.

To sum up the treatment of Pott's paraplegia I would suggest that the first step is that the patient should be transferred without delay to a first-class orthopædic centre, where there is every facility for open-air treatment, for orthopædic care and for operation under the best circumstances by a surgeon skilled and experienced in spinal tuberculosis.

In most of the minor and some of the moderate cases conservative treatment suffices, for the paraplegia after a short time progressively fades away. But in a moderate degree of paraplegia, which does not begin to show progressive signs of amelioration within a few weeks, decompression is indicated. Costotransversectomy and laminectomy without facetectomy, are operations of relative safety. Costotransversectomy with thorough evacuation of a paravertebral abscess may have to be repeated or followed by laminectomy through another route if there is no amelioration within three or four weeks. First-class radiography, sometimes with tomography, facilitates the choice.

I would say that there is ordinarily no indication for lateral rhachotomy in "early" paraplegia. But it is most valuable when decompression is indicated in early (or late) paraplegia after posterior spinal graft fusion.

For then approach to the theca through laminæ immensely thickened into one continuous mass is exceedingly dangerous to the cord, and lateral rhachotomy is much safer; furthermore, the stability is assured by the posterior spinal fusion which the operation leaves undisturbed.

In "*late*" *paraplegia* lateral rhachotomy has many virtues, and almost all where there is extreme angulation. Though the operation is extensive, delicate, and cannot be hurried the patient is no longer ill with an invasive and destructive disease, and, therefore, no longer an unfavourable subject for such an operation. Furthermore, in most cases stability is assured and the series of lateral articulations on one side can, therefore, be interrupted without fear.

In true cases of late onset paraplegia, unaccompanied by any local recrudescence of disease, such as occasionally account for cases in this group, the paraplegia is associated with prolonged stretching combined with movement over a sharp angle or ridge. While lateral rhachotomy can provide access for the relatively extensive procedure necessary to give the cord a smoother and shorter path. Yet even when it has been done with the utmost delicacy, without damage to the pleura, or to the vascular supply of the cord, the result may be utterly disappointing because irreversible degenerative changes already exist.

So we are brought back to the conviction that the early diagnosis of spinal tuberculosis and its prompt, effective and complete treatment are the only means of preventing extensive destruction and severe angulation, leading perhaps to irreparable paraplegia.

The author wishes to acknowledge most gratefully the help of Professor Norman Dott and Mr. G. L. Alexander in lending illustrations; and of Mr. Norman Capener and Mr. E. W. Somerville.

He wishes to thank also the Editor of the *Proceedings of the Royal Society of Medicine* for the loan of blocks.

## REFERENCES

1 POTT, PERCIVALL (1779) Remarks on that kind of Palsy of the Lower Limbs which is frequently found to accompany a curvature of the spine, and is supposed to be caused by it, together with its method of cure; (1782) Further Remarks on the Useless State of the Lower Limbs in consequence of a Curvature of the Spine.

2 GIRDLESTONE, G. R. (1940) *Tuberculosis of Bone and Joint.* Oxford University Press.

3 MANN, K. J. (1946) *Lancet* **2**, 744.

4 ROLLIER, A. *Personal Communication.*

5 GIRDLESTONE, G. R. (1937) *Trans. Med. Soc. Lond.* **60**, 199.

6 BUTLER, R. W. (1935) *Brit. J. Surg.* **22**, 738.

7 SEDDON, H. J. (1935) *Brit. J. Surg.* **22**, 769.

8 SOMERVILLE, E. W. *Personal Communication.*

9 ALEXANDER, G. L. (1946) *Proc. Roy. Soc. Med.* **39**, 730.

10 SEDDON, H. J. (1946) *Proc. Roy. Soc. Med.* **39**, 723.

11 CAPENER, N. *Personal Communication.*

# THE PATHOLOGY OF BLUNT HEAD INJURY

Lecture delivered at the Royal College of Surgeons of England
on
19th November, 1948
by

Keith Simpson, M.D., Lond.
Reader in Forensic Medicine to Guy's Hospital in the University of London

SO MANY ASPECTS of blunt injury to the head might usefully be discussed that it would be unprofitable to make an extensive survey in a single lecture. I am going to assume much that is familiar knowledge in devoting attention to certain aspects of head injury the nature and pathology of which have recently become clarified, and which are of sufficient clinical significance to merit special attention.

No clear conception of the nature of head injuries can be achieved without some reference to both the anatomy of the parts and the dynamics of injury which Holbourn, the Oxford physicist, has so brilliantly applied to its conception.

## ANATOMY

The rigidity of the skull in adults is quite remarkable, the buttressed arrangement of the base and form of the calvarium having fine architectural strength. The cranium does not change shape upon impact so long as the head is free to move, and requires enormous weight to depress its wall when held still and compressed. It escapes fracture in about one-quarter of all fatal cranio-cerebral injuries.

On the other hand, its content of brain with its vast bed of blood vessels and the cerebro-spinal fluid system is at once a highly labile and delicate structure. Much of the danger is averted by the mobility and tortuous course many of the vessels pursue, but the extra dural arteries, the rigid-walled dural sinuses, and the perforating veins which run across the subdural and subarachnoid space are "fixed" to varying degree and, as elsewhere in the body, fixation introduces the danger of stretch and rupture if the brain lags inside a twisting skull. Though the arachnoid tetherings may to some extent lessen this danger, they cannot eliminate it. Further, whereas the dura is likely, by its dense adhesions to the interior of the skull to limit venous, if not arterial, bleeding, the space between dura and arachnoid or arachnoid and pia has no such quality, blood escaping freely between these layers. The localisation of bleeding outside the dura, from meningeal arteries or their venæ comites, has one unfortunate consequence—the local bulge resulting in displacement of adjacent brain and serious increase in intra-cranial pressure.

The arachnoid is a fragile membrane, almost certain to tear upon any substantial trauma, and to admit subarachnoid fluid and blood to the

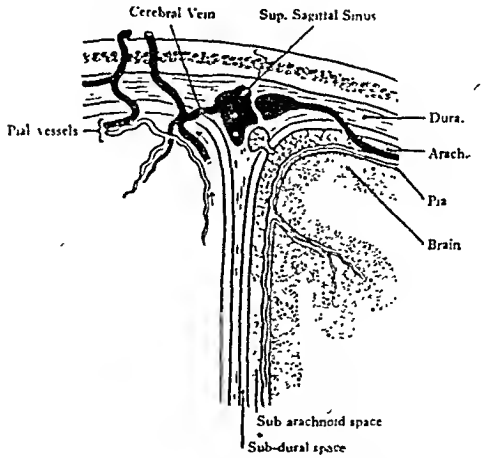



Fig. 1. A coronal section through the vault region of the skull showing relation of perforating vessels to membranes and brain (after Gray).

subdural spaces. The relative avascularity of these has resulted in a curious anomaly, the chronic subdural hæmatoma, first recognised by Trotter to be always traumatic. I shall refer to these matters again in describing their pathology.

As regards the brain, the exposed nature of the soft grey surface matter with its penetrating network of small vessels makes cortical contusion with disruptive hæmorrhages one of the commonest of all events. Lag in acquiring rotating motions of the head is particularly productive of injury to the surface of the brain as it is dragged across the rough prominences of the interior of the skull. Adhesions between the membranes and such injured surfaces upon healing are capable of a legion of evils —epilepsy, cysts, circoid aneurysmal vessel masses, obstructed cerebro-spinal fluid flow, meningitis serosa circumscripta, internal hydrocephalus. The anatomy of the brain and its membranes gives latitude for healing but the delicacy of the cerebro-spinal fluid drainage system and the close proximity of the cortex makes any reparative process pregnant with danger.

## MECHANICS

The loose medical inferences drawn for so long in explanation of the pathology of blunt head injury—of concussion and contusion of the brain in particular—have recently been put into Newtonian order by Holbourn, the research physicist at Oxford (1941). He pointed out that the skull and its contents, when subject to physical force, were likely to behave just as any other physical body and suffer damage from exactly similar stresses. The changes that followed later—hæmorrhage, œdema, vascular stasis, changes in the circulating blood volume and pressure—are to be put clearly on one side as consequences of injury : it is surprising how long these secondary changes were thought to account for concussion, which was of instant occurrence.

Holbourn sets out the chief physical attributes of the brain and its coverings as follows:

1. *The skull is, in adults, so rigid that, until fractured, deformation is not a significant factor.* The older conception of the cranium becoming momentarily egg-shaped upon impact is plainly untrue: it may do so only if fixed—an uncommon event in practice. Injury to the brain by such momentary flattening does not occur, and is not, therefore, an acceptable explanation of contre-coup.

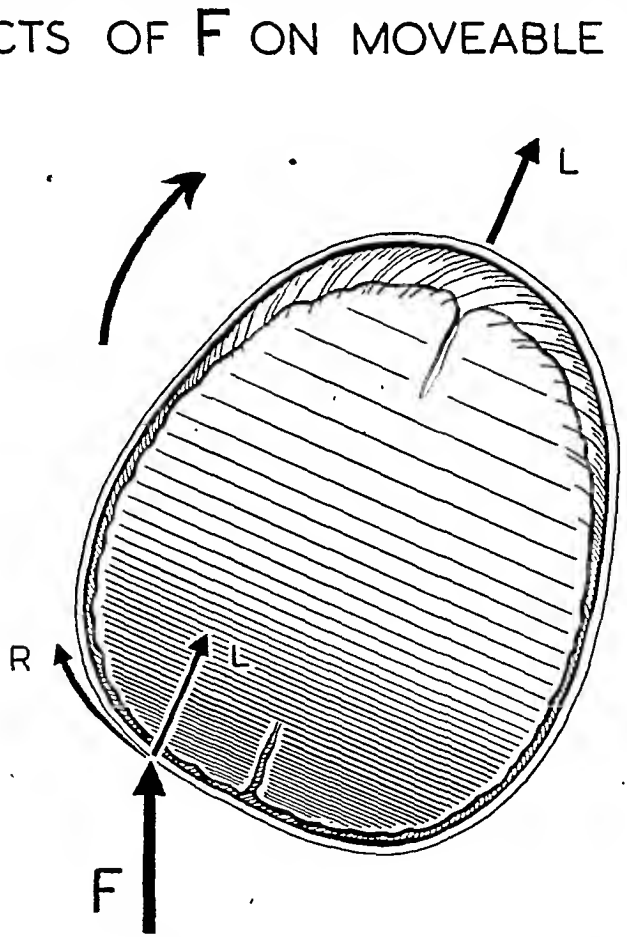



Fig. 2. Effect of force F on moveable head, causing linear and rotational strains.

2. *The brain, cerebro-spinal fluid and blood vessels are of uniform density*, so, although subject to slight "lag" in movement (both linear acceleration/deceleration and rotation), the conception of the denser brain floating mobile in cerebro-spinal fluid and capable of rolling about loosely within the cranium has also to be abandoned. Slight linear lag, whilst inertia is being overcome, is a minor operative factor.

3. *The brain is remarkably incompressible* as a whole, though it has a very low "modulus of rigidity"—*it is easily deformed.* Depressed bone fragments or accumulating blood will easily deform it locally, flatten the convolutions generally or press the brain stem into the foramen magnum, but not *compress* it.

Strains of a stretching or twisting (shear) kind are the chief danger, and may plainly affect any part, though (as Greenfield suggested (1938)), the fixing of certain parts like the brain stem, held in the incisura tentorii, promotes local stretching or tearing injury. Holbourn adds, from his experimental experience of the distribution of surface injury due to rotation strain, that the anatomy of the interior of the skull adds a second important "fixing" factor. As the brain lags on rotation of the skull (like wool in a rotated bottle of water) it becomes chafed against the prominences of the interior of the skull, over the wings of the sphenoid and the roofs of the orbits.

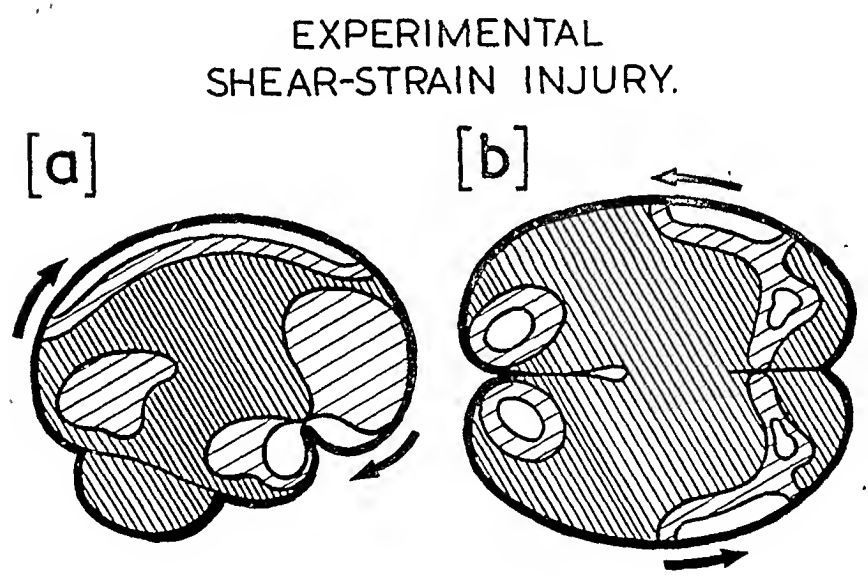



Fig. 3. Effect on brain surface of blows causing rotation of skull. (Finest shading represents least surface contusion after Holbourn, 1941.)

The distribution of experimental contusion of jelly brains in wax skulls agrees to a remarkable extent with these premises.

Le Count and Apfelbach (1920) and Vance (1927) had appreciated that, in order to sustain contusion, the head must be free to move upon impact. Neither petechiæ nor surface contusion (local or contre-coup) will appear if the head is fixed. Twisting strains operated throughout the brain. Linear acceleration strain was plainly of less significance, but must operate while the inertia of the brain is being overcome.

Russell (1937) showed that it was the *rate* of such physical changes which was of most importance and envisaged a kind of stretching rarefaction of the tissues over the opposite surface of the brain whence the skull had already moved away. Acceleration or deceleration, if violent, produced a transient but damaging rarefying stretch on the opposite surface.

It was this which accounted for the more pronounced surface tearing and "contusion" on the side opposite impact which was described as "contre-coup." Symmetry is observed even in the individual convolutions (Holbourn and Courfield).

Fig. 4. Distribution of bruising by contre-coup showing more pronounced injury in R. frontal region following impact to L. occiput.

Almost every injury causes both acceleration/deceleration *and* rot strains, and it matters not, of course, whether the head is forced t by some impact or forced to come to rest by striking an uny surface. The mechanics of injury remain the same. The *mon* must be sufficient and the *rate* of the physical change sufficiently

Holbourn's work is of great importance, for it clarifies an issue which has been obscure over a century of study. It provides factual knowledge

(of physical properties) which conform to the known facts of brain injury and affords a plain explanation for them.

## PATHOLOGY

Something must be said first of the form of head injury which results in functional loss—concussion—but which has caused much confusion because (*a*) it appeared to be completely recoverable and (*b*) no structural change was found. It is curious that, though, as the condition of "punch-drunk" reveals, concussion is not completely recoverable even in its least damaging form, it should not be accepted as certain that damage must have taken place, whether it could be seen or not.

1. *Function* may be impaired without visible change as in the vagal inhibitory reflexes which interfere with cardiac or respiratory rhythm, or in states of anæsthetisation.
2. *Damage* may be evident functionally, concussion and loss of reflexes ensuing without histological evidence of tissue changes (Miller, 1927). Stretched nerves or strained synapses may give no evidence of their deteriorated functional state upon even intra-vitam trypan blue staining, though Rand and Courville (1934), have demonstrated stretched nerve fibres. It is not certain that some structural change will be found even though damage has occurred.

Both Polis (1894) and Vance (1927) observed that lesions were not always apparent in even fatal concussion. In 16 out of 512 fatal head injury cases Vance found nothing, and I have, among records of similar cases, one in which, though a crushing blunt scalp lesion was present behind the R. ear, no fracture, contusion or neck injury was found. The subject was found dead on London Bridge, and I had a strong suspicion that he had been sandbagged from the character of the scalp injury. Denny-Brown and Ritchie-Russell (1941) have shown that identical conditions can be reproduced experimentally in various animals.

The confusion which followed from the study of the consequences of such trauma—circulatory stasis (Schaller, Tamaki, Newman), arterial spasm (Kocker), œdema (Hassin), petechial hæmorrhages, first described by Richard Bright and since by innumerable authors—is now becoming dissipated. These are results: no one could for a moment suggest they were responsible for the immediate loss of consciousness which ensues upon the head being struck.

The natural consequence of any injury to live tissues is reaction to damage, exudation, œdema, vascular dilatation (after momentary contraction) and, in the event of tearing of vessels, bleeding. Where this develops and how it spreads depend upon the site and character of impact and the anatomy of the injured tissue. Certain common forms of pathology deserve special consideration:

(*a*) *Extra-dural hæmatoma.* The only common situation for this important surgical—and medico-legal—lesion is the temporal vault, over a half of all (54 per cent. in Rowbotham's series of 33 surgical cases) clots lying in this situation. The majority arise from tears in the branches of the middle meningeal artery, but some are due to tears in the dural sinuses or trans-dural veins. My own experience is that such hæmorrhages occur about as frequently with fracture as without. I have twice seen boxing knock-outs, one insufficient to call a full count, cause fatal extra-dural hæmorrhage during the following few hours. The lucid period may vary from two or three hours to as much as a day, especially when it is the venæ comites rather than the artery which bleed. It fails to appear in a third of the cases (Melchior and Tietze, 1916).

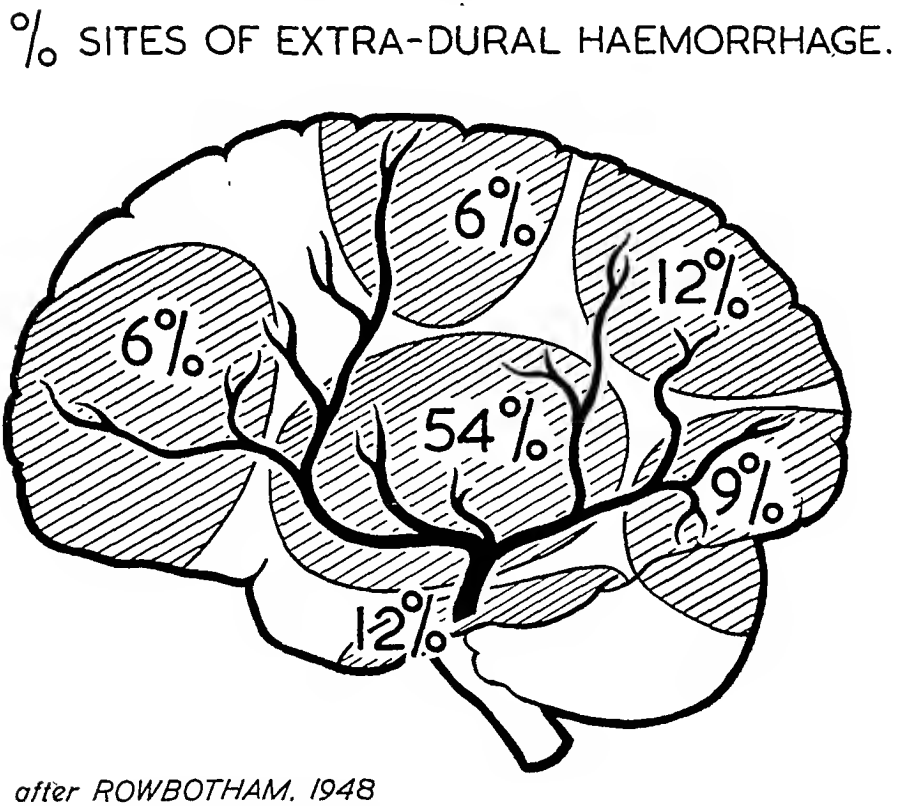



Fig. 5. Distribution of extra-dural hæmorrhage in relation to middle meningeal artery.

To the surgeon the classical course of events is diagnostic. To the medical jurist the sequence of events has another significance. The lucid period may disarm suspicion as to the seriousness of an injury where shortly prior to ultimate loss of

consciousness some new injury arises. One such death was attributed to a minor scuffle in a public house when, in fact, the victim had some 10 hours previously fallen from his bicycle to a concrete path sustaining a bruised scalp, lightly contused brain and ruptured middle meningeal artery.

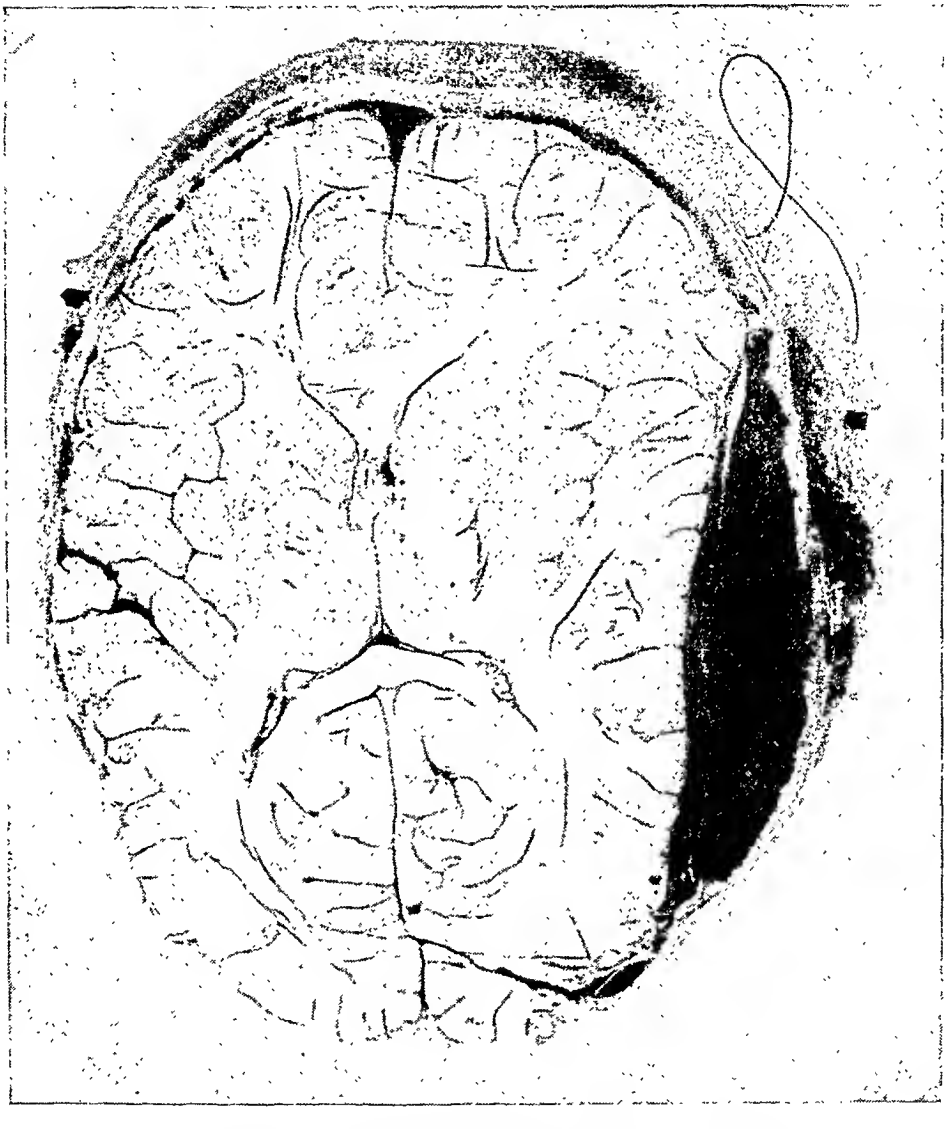


Fig. 6. Fractured temporal vault causing tear of middle meningeal artery and extra-dural hæmorrhage.

The pathology—and the surgical prognosis—may, unfortunately, be complicated by contre-coup brain contusion with subdural bleeding, or by deeper brain injury which may prove fatal in spite of successful extra-dural surgery.

Extra-dural hæmorrhage is rare in infants for two reasons. The dura is much more tightly attached to the interior of the skull vault—as any pathologist used to stripping it will agree—and the skull as a whole has not yet acquired the brittle rigidity which encourages fissure fractures so likely to tear the vessels. The dense adhesion of the dura to the skull increases again with advancing years.

(*b*) *Sub-dural hæmorrhage*, the commonest of all forms of bleeding owing to the many sources of vascular trauma, spreads freely in in all directions, though commonly remaining more or less confined to one-half of the cerebral space.

The remarkable pathological feature of this lesion is the development, without symptoms, of the encysted sub-dural hæmatoma in the temporal or parietal region, usually (Hanke, 1939) in elderly subjects.

Leary (1934) has pointed out that the slow rate of absorption of blood from this space is due to the fact that it has no vascular lining, only the dura with its limited capacity taking part in the process. A kind of false membrane rapidly forms on the arachnoid surface of the clot, and within 24 hours may start a proliferative process including the rapid development of giant capillary vessels.

Recurrent bleeding into these is not uncommon, in spite of the absence of further injury. The capillary vessels may ooze—being encouraged to do so by a rising osmotic tension in the cyst content after the first three weeks.

Trotter's insistence that all such cysts were traumatic is undoubtedly true, though a history of trauma *followed by significant symptoms* may be lacking.

(*c*) *Traumatic sub-arachnoid bleeding*. It is important to recognise the common natural sources of bleeding into this space—usually the ruptured developmental cerebral aneurysm. When less patient search has failed to reveal a source, trauma has all too commonly been introduced as a possibility—quite without basis.

Injured pial vessels and their cortical branches, torn or crushed by cortical contusion, provide the usual traumatic sources, and the parallel of Holbourn's researches on the mechanism of contusion has greatly simplified the conception of their nature. Torsion and surface contusion by shear during the period of lag when the head is set in sharp rotation—or suddenly decelerated—are the operative forces. Some symmetry may be shown in the degree of affection of cortical convolutions (Holbourn) and the surface involved may be very widespread, adding to the difficulties of effective surgery.

(*d*) *Deep brain contusions*, arising from the same linear and shear strains, may vary from minute petechiæ to substantial hæmorrhages, and be situated anywhere in white or grey matter.

The widespread petechiæ of blast lesions and the cortical, white, nuclear and ventricular hæmorrhages of violent blunt injury are well recognised. J. G. Greenfield (1938) envisaged the heavy cerebral hemispheres moving on the more fixed brain stem, stretching it over the incisuræ of the dura, and there is no doubt that brain distortions are a common source of pontine and bulbar hæmorrhagic splits. Denny-Brown and Ritchie-Russell (1941) regarded the brain stem and upper cervical cord segments as the commonest site for contusions of this type, and it seems reasonable to suppose that sub-microscopic lesions in the same situations occur in concussion. In experimental work all brain stem reflexes are paralysed at once by concussion. Secondary changes like myelin fibre swelling, œdema, foci of anoxic degeneration, sometimes with small local thromboses—especially in Ammon's horn (Rand and Courville, 1934)—are all conditions whose development might rest solely with circulatory disturbances. They have been observed repeatedly with experimental anoxia, and might reasonably be expected as a consequence of the widespread trauma of brain contusion due to the stresses outlined. They are *not* the cause of concussion. Post concussional symptoms may reflect the development of these areas and of microglial invasion and sclerosis in specially vulnerable areas. Epilepsy is a recognised consequence of cortical scars and encephalopathy of "punch-drunk" type, or causing Parkinsonism, may also occur.

No subject in the realms of trauma has received more enlightenment in recent years than this, and it is an excellent example of the value of applying the basic sciences to medical study. It is, in the fair prosecution of the criminal law, of the greatest importance that the precise manner in which injury to the head was sustained should be known—that reconstruction should be secure and absolutely fair.

## REFERENCES


BRIGHT, RICHARD (1831) *Reports of Medical Cases*, Vol. 2, Pt. I.
COURVILLE, C. B. (1942) *Arch. Surg.* **45**, 19.
DENNY-BROWN, D., and RITCHIE-RUSSELL, W. (1941) *Brain* **64**, 93.
GARDNER, W. J. (1932) *Arch. Neurol. Psychiat.*, Chicago **27**, 847.
GREENFIELD, J. G. (1938) *Proc. Roy. Soc. Med.* **32**, 43.
HANKE, H. (1939) *Ergebn. Chir. Orthop.* **32**, 1.
HASSIN, G. B. (1940) *Injuries of Skull, Brain & Spinal Cord.* Ed. S. Brock, London.
LEARY, T. (1934) *J. Amer. Med. Ass.* **103**, 897.
LE COUNT, E. R., and APFELBACH, C. W. (1920) *J. Amer. Med. Ass.* **74**, 501.
MELCHIOR, E. and TIATZE, A. (1916) *Neue deutsche Chirurgie.* Stuttgart, Enke. 18.
PENFIELD, W. (1938) *Arch. Neurol. Psychiat.*, Chicago **40**, 41.
POLIS, A. (1894) *Rev. Chir.* **14**, 273.
RAND, C. W., and COURVILLE, C. B. (1934) *Arch. Neurol. Psychiat.*, Chicago **31**, 526.
RITCHIE-RUSSELL, W. (1932) *Brain* **55**, 549.
ROWBOTHAM, G. F. (1948) *Acute Injuries of the Head.* London.
SCHALLER, W. F., TAMAKI, K., and NEWMAN, H. (1937) *Arch. Neurol. Psychiat.*, Chicago **37**, 1048. (1941) *Ibid.* **45**, 1.
SCOTT, W. W. (1940) *Arch. Neurol. Psychiat.*, Chicago **43**, 270.
TROTTER, W. (1914) *Brit. J. Surg.* **2**, 270.
VANCE, B. M. (1927) *Arch. Surg.* **14**, 1023.

# HIGH VOLTAGE X-RAYS IN THE TREATMENT OF MALIGNANT TUMOURS AT A DEPTH

Lecture delivered at the Royal College of Surgeons of England

on

18th October, 1948

by

D. W. Smithers, M.D., M.R.C.P., D.M.R.
Professor of Radiotherapy in the University of London
Director of the Radiotherapy Department of the Royal Cancer Hospital

## General Problems in Cancer Treatment

THE PROBLEMS ASSOCIATED with cancer, as though not inherently difficult enough already, are made worse by a combination of circumstances affecting the patient, his doctor and the specialist to whom he sends him for treatment. As 70,000 people die from cancer each year in this country alone many members of many households come to dread its consequences through direct, unfortunate personal experience. It is not surprising that the sound of the word cancer acquires a sinister significance and leads either to fear or a sense of resignation, both of which may disincline a patient to consult his doctor. A general feeling of hopelessness even attacks doctors at times, and nothing so quickly removes that alertness and sense of urgency which leads them to suspect the possible significance of the apparently trivial. There are as yet, for all our notions and nostrums, only two curative methods of treatment known, surgery and radiotherapy, both highly specialized pursuits requiring such concentration of effort and training for proficiency that it leads inevitably to a bias in favour of the direction in which that effort has been made. This, with the added tendency towards further specialization within both surgery and radiotherapy, sometimes results in a patient who thinks that he is putting himself in the hands of a specialist finding himself in the hands of a technique. The difficulties are not lessened by the fact that the most successful treatment quite often requires a combination of both surgery and radiotherapy. There is, therefore, considerable difficulty even in ensuring that each patient takes full advantage of the best possible treatment that is available for him.

The main inherent difficulties, the occasional lack of all symptoms until the disease is already far advanced and the absence of any available means of controlling the disseminated disease, await the discovery of a specific cancer test and a specific cancer cure for their solution. Much effort, time and money are spent in this search for " a test " and " a cure." While we lack knowledge of the nature of the fundamental change that takes place in a cell when it becomes cancerous, perhaps something akin to the knowledge of life itself, we cannot be sure either that such a change in comparatively few cells will ever provide material for a specific test for early cancer, or that a selective lethal action on all disseminated

malignant cells will ever result from the administration of any special substance. The lack of specificity of the toxic substances at present in use, like the chloroethylamines, for instance, which can and do produce some tumour regression at times, is seen all too clearly when we turn for a moment from concentration on the tumour to examine other tissues, such as the bone marrow. Changing the response of the body to the new growth within it or influencing the vitality of the neoplasm itself by means of alterations in endocrine balance leading to delay in progress or even temporary arrest of the growth, as may occur with cancer of the prostate and cancer of the breast, would seem to indicate a hopeful line for progress. We can, however, now deal efficiently and effectively with the problem of localized cancer when it comes our way, by means of surgery and radiotherapy, and we should try to arrange that it shall come our way more often. By far the best method of achieving the second objective is to concentrate upon the first. If we cure the patient with early cancer, and the public and the doctors know that we do this, more early cancer will be there to be cured. Not all that we would wish for, because of the factors as yet beyond our control, but probably quite as much as we are at present equipped to deal with adequately.

The problems can be simplified at once by ceasing to speak of the heterogeneous group of tumours concerned as a whole and narrowing the discussion to specific types of tumour occurring at definite sites. Every doctor knows the difference in prognosis between a basal-cell carcinoma of the nose and a columnar-cell carcinoma of the stomach; if the first is not cured it is usually due more to the failure of the doctors than the neglect of the patient, and if the second is cured it is often due as much to a fortuitous set of fortunate circumstances as to the skill of the medical profession. Not every doctor is so familiar with the more subtle differences in prognosis that exist between tumours of the posterior and anterior segments of the laryngeal ventricle, for instance, between tumours of the hard and soft palate, or between an ulcerating anaplastic carcinoma of the anterior rectal wall and a protruberant differentiated carcinoma of the posterior rectal wall. In general, however, the malignant tumours which are successfully dealt with in a substantial proportion of the cases seen in hospital are the accessible ones, predominantly the squamous-cell carcinomas of the skin, lip, mouth, larynx and cervix uteri and the adenocarcinomas of the breast. These conditions are now curable in a high proportion of all cases seen, because the patients reach hospital in sufficient numbers while the disease is still localized and because the extent of the tumours can be fairly readily defined and adequate surgery or radiotherapy applied.

Patients with inaccessible or deep-seated tumours are also curable in the early stages, but are seen so seldom in hospital while their tumours are still localized enough for successful removal by surgery or destruction by irradiation that few are in fact saved. Early cancer is curable, the trouble is that it is not more often diagnosable. Those who persistently

complain that the present treatment of cancer is unsatisfactory, and who are always looking for some universal cure, might profitably consider the not entirely unreasonable proposition that the treatment of cancer has already made such progress that patients with early tumours may now be cured almost wherever the tumour may appear, and that the reason that more patients are not cured is that the diagnosis of cancer lags so far behind the treatment. Where diagnosis is simple, as in cancer of the skin, for instance, treatment is already so successful that no "cancer cure" could be expected to produce much improvement. A little pride in the undoubted achievements of both surgery and radiotherapy in this field is permissible, and a show of it may raise the spirits of a patient here or a doctor there and so provide another early case for cure.

## Treatability of Deep-seated Tumours

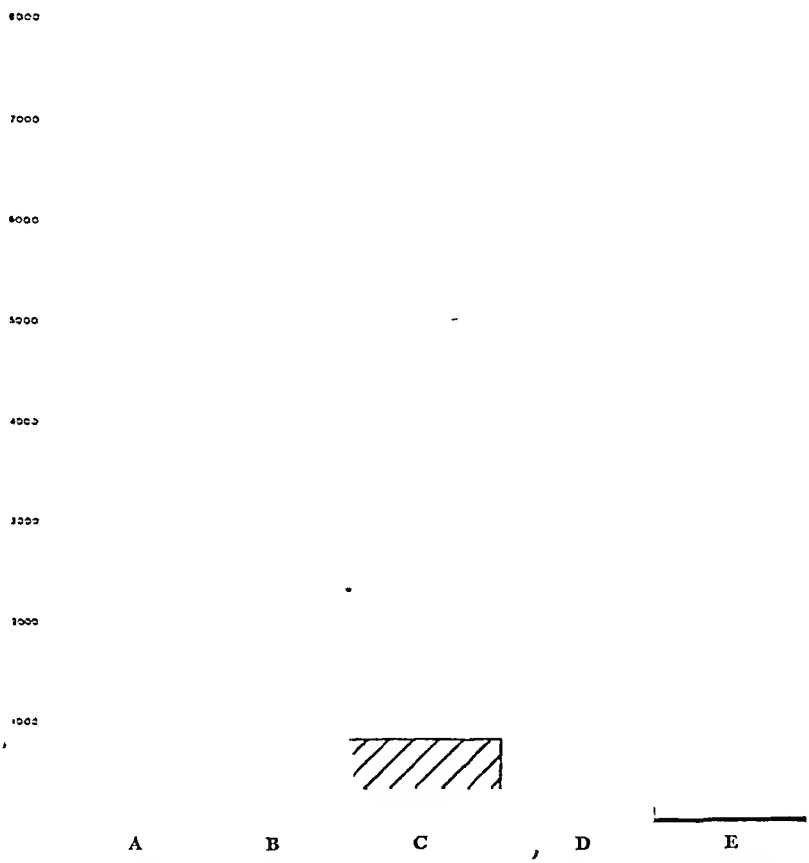
There are no adequate morbidity figures available in this country for malignant disease, but we may speculate on the number of cases of cancer at various sites that occur each year and the proportion of these which at present receive a form of treatment which is designed at least to make an attempt at cure, and not merely to produce temporary palliation. These speculations are based on available evidence, such as the mortality figures from the Registrar-General's report, MacKenzie's (1939) investigation into the extent to which patients with cancer receive treatment, the figures published from the larger treatment centres, and the cases seen and treated in one's own hospital. Taking a leaf from those learned sociological reports which *The Times* referred to recently as "all graphs and guesswork," two such speculations are presented for carcinoma of the lung (Fig. 1) and carcinoma of the œsophagus (Fig. 2). A more optimistic guess for carcinoma of the stomach (Fig 3) published by Taylor (1948) is also given as an example. We know that any treatment holding out even a remote prospect of cure is comparatively seldom administered to patients with deep-seated cancer, and that the failures that do occur when attempts at cure are made are, even then, due more to the spread of the disease than to any other single factor. Any means of localizing tumours, of rendering them less active and of reducing the risk of dissemination during attempts at removal are, therefore, of the greatest importance.

## Surgery and Radiotherapy

Radiotherapy is established as a means of removing tumours in its own right, and for many accessible sites and most sensitive tumours is to be preferred to surgery. Avoidance of mutilation, diminution of the risk of dissemination, and a steady improvement in technical skill and accuracy in the application of radiation have been chiefly responsible for the advance of this method. Few doctors with experience of adequate radiotherapy would now advise a glossectomy for carcinoma of the tongue except possibly for a small primary limited to the tip, or in a patient who

## CARCINOMA OF THE BRONCHUS

**Estimate of number of cases per annum in England and Wales. Number treated and number surviving five years. (Based on figures for 1945.)**




A. Annual incidence estimated at 8,000 cases. 7,553 deaths registered in 1945. (May be a considerable underestimate.)

B. Number treated each year estimated at 1,000. Mackenzie (1939) estimated that 26 per cent. of patients dying with cancer had been treated. and only 5 per cent. with carcinoma of the Bronchus. (Proportion has increased but may still be an overestimate.)

C. Number treated by radiotherapy estimated at 850. (Palliative treatment only 500, attempt at radical 350.) (Radical treatment may be overestimate.)

D. Number treated by surgery estimated at 150 (15 per cent. of all cases treated), excluding exploration without removal. (May be overestimate.)

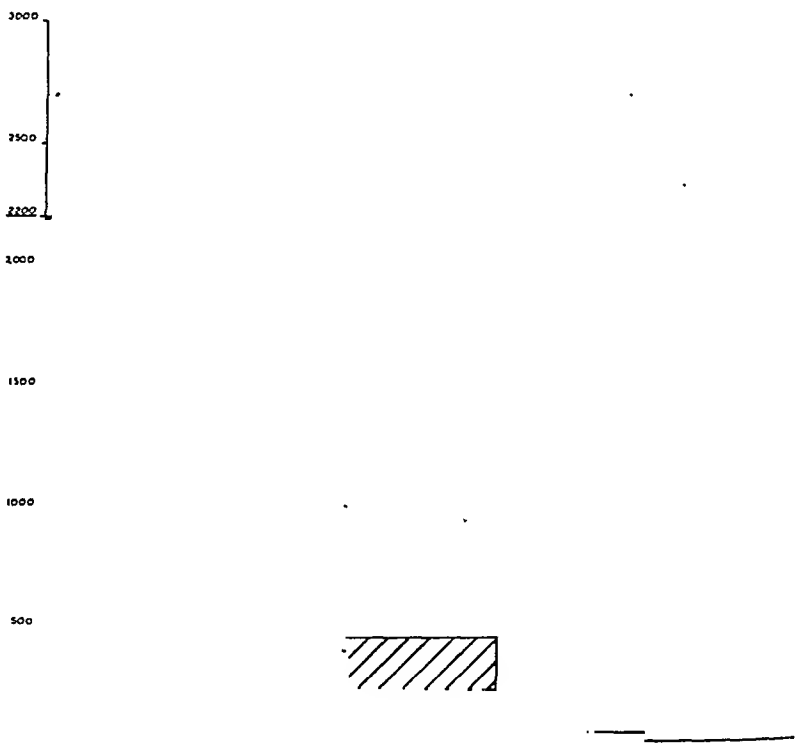
E. Number surviving five years estimated at 25 cases. (2·5 per cent. of all cases treated.) (Probably an overestimate.)

Fig. 1.

## CARCINOMA OF THE ŒSOPHAGUS.

Estimate of number of cases per annum in England and Wales.

Number seen in hospital, number treated and number surviving five years. (Based on figures for 1945.)




A. Annual incidence estimated at 2,200 cases. 2,268 deaths registered in 1945. (Probably [illegible] accurate. May be slight overestimate.)

B. Number seen at treatment centres each year estimated at 1,000. (Probably fairly [illegible] accurate.)

C. Number treated by radioth [illegible] 450. (Palliative treatment only 220, attempt at radical 230.) [illegible] nated that 21 per cent. patients dying with carcinoma of [illegible] treated. (May be overestimate.)

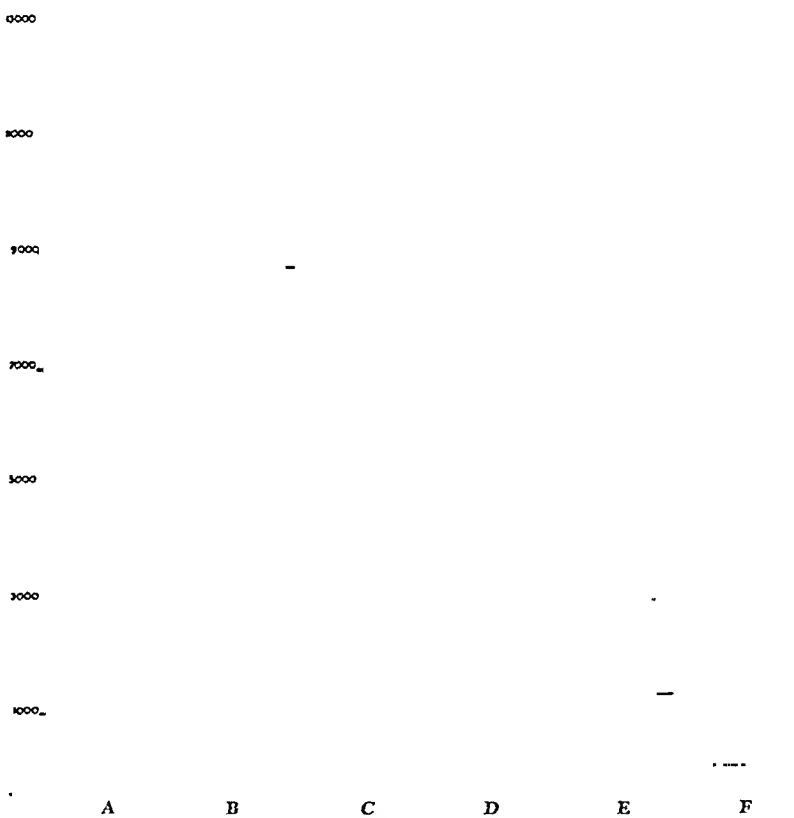
D. Number treated by surgery estimated at 50. (Number increasing now (1948) but probably overestimate for 1945.)

E. Number surviving five years estimated at 10 cases. (Probably an overestimate.)

Fig. 2.

## CARCINOMA OF THE STOMACH

**Approximate fate of patients in England in 1938. (After Taylor. Lancet 1948. 1, 581.)**




A. Annual incidence estimated at 13,000.
B. Number referred to hospital each year estimated at 8,750.
C. Number investigated by Laparotomy estimated at 4,400.
D. Number in which growth is removed estimated at 1,750.
E. Number surviving operation estimated at 1,250.
F. Approximate number surviving at five years estimated at 850.

Fig. 3.

had developed a malignant tumour on a syphilitic base. It is becoming increasingly difficult to maintain that total laryngectomy or Wertheim's hysterectomy are still to be preferred in cases that are suitable for radiotherapy. At other sites and with particular types of tumour radiotherapy has become an equal partner with surgery, and their happy combination has vastly improved the results that can be obtained. There can no longer be any doubt that the surgeon and the radiotherapist can together do more for patients with carcinoma of the breast or seminoma of the testicle, for instance, than either can do alone. If we look at the groups of patients that we see with these two diseases as a whole, and not in small selected samples, it can reasonably be maintained that the surgeon, by co-operation with the radiotherapist, has more than doubled the survival rates. At many of the deep-seated tumour sites, however, surgery has advanced alone. It is important that we should know whether radiotherapy has anything of value to offer here as well.

Lack of success with radiotherapy by itself for deep-seated tumours has been partly due to the fact that few curable cases report to hospital, and that nearly all of those that do are treated surgically. That radiotherapy is capable of eradicating accessible tumours of similar structure to some of those met with at a depth, has been amply demonstrated and that it may at times deal successfully with deep-seated tumours is well known, at least to radiotherapists. We have, for example, four patients who are alive, or who lived for more than five years, following X-ray treatment to squamous-cell carcinomas of the œsophagus: one lived nine years, one lived eight years, one over six years, and one is still alive over five years. Five other patients of ours who died with metastases from carcinoma of the œsophagus were found at post-mortem examination to have no sign of any residual primary tumour. The published reports of five-year survivals, following radiotherapy in proved cases of carcinoma of the œsophagus, still well exceed in number those following surgery, despite the selection of suitable cases for operation and the advances in surgical technique that have taken place. We have two patients who lived more than seven years after X-ray treatment to proved carcinomas of the lung, and another who is alive and symptom-free just under five years after treatment. Similar reports from elsewhere are to be found in the literature, despite the even more rigid selection of suitable cases for surgery that has occurred at this site. The results obtained with surgery alone for many deep-seated tumours are not so good that we can afford to neglect any help that radiotherapy may have to offer.

There are also a number of technical reasons why radiotherapy has not been more successful in these situations in the past. A beam of radiation, generated at the voltages that we have been accustomed to in radiotherapy, gives up energy on entering the tissues in such a way that there is a steady diminution in the dose delivered to points situated at increasing depths (Fig. 4). The nearer a tumour is to the surface,

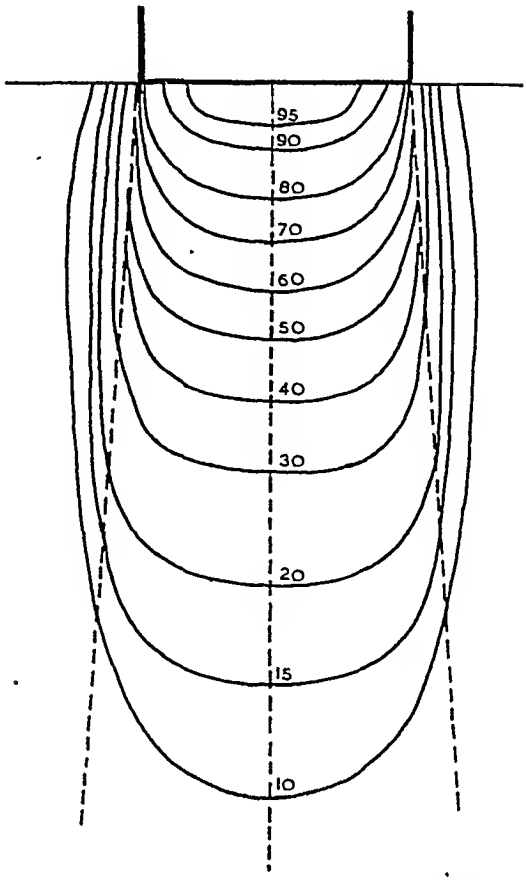



Fig. 4. 400 kV. isodose curves. Chart for a 7 cm. diameter field. Lines joining points receiving the same percentage depth doses.

therefore, the easier it is to localize the destructive effect of the radiation to the tumour volume, and to spare the normal tissues. In the treatment of deep-seated tumours special techniques are adopted to increase the tumour dose that can be given, such as the use of multiple beams of radiation or rotation of the patient or the beam during the treatment period (Fig. 5). The introduction of higher and higher voltages and the construction of new apparatus for accelerating particles has now provided beams of radiation which give a greater dose at a depth than on the surface. The emission of secondary radiation within the body builds up the energy to a maximum at a point below the surface, the position of which depends on the characteristics of the primary beam, before allowing the usual fall off with depth because of absorption. At 2-million volts the maximum dose is situated at a depth of approximately 0·5 cm., at 20-million volts at about 2 cm., at 50-million 7 cm., and at 100-million 10 cm. (Fig. 6) (Charlton & Breed, 1948). It is possible to use multiple field or rotation techniques with these high-voltage beams as well so that very high localized tumour doses at a depth are coming

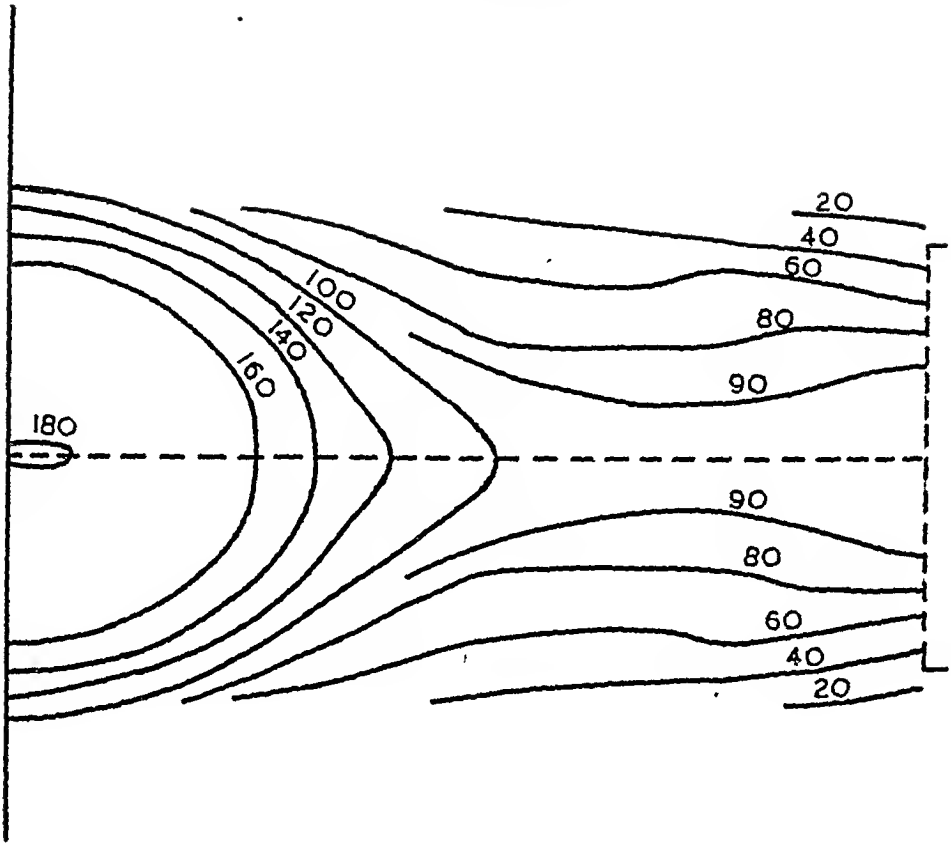



Fig. 5. Rotation distribution. 400 kV. 50 cm., f.s.d., 7 cm. diameter circular field, represented by the dotted line on the right rotating in a horizontal plane around a circle with a 15 cm. radius.
The three dimensional distribution of the radiation is obtained by rotating this diagram about the vertical line on the left.

into the field of practical treatment (Figs. 7 and 8). The problem now is rather one of localizing the extent of the volume occupied by the tumour so as to know accurately where the radiation is required than of finding a means of delivering a high enough dose at a depth. The biological investigations carried out so far do not suggest that we may expect any great divergence, up to 5 MeV. at least, from the effects produced by radiations in the energy range at present in use. The risks of damage to normal tissues at a depth will, however, be considerable, fortunately we are far better equipped to control dose distribution and far more aware of the dangers than were those who originally developed X-ray therapy in the 100-200 kilovolt range, and teleradium with 1-5 gramme units. Nevertheless, progress will only be made by taking some risks, and some damage is almost certain to occur in the path of experience. We must see that this time the hospital physicists, who are now available to guide us, have adequate opportunities for full investigation of the new dosage problems before extensive clinical trials are

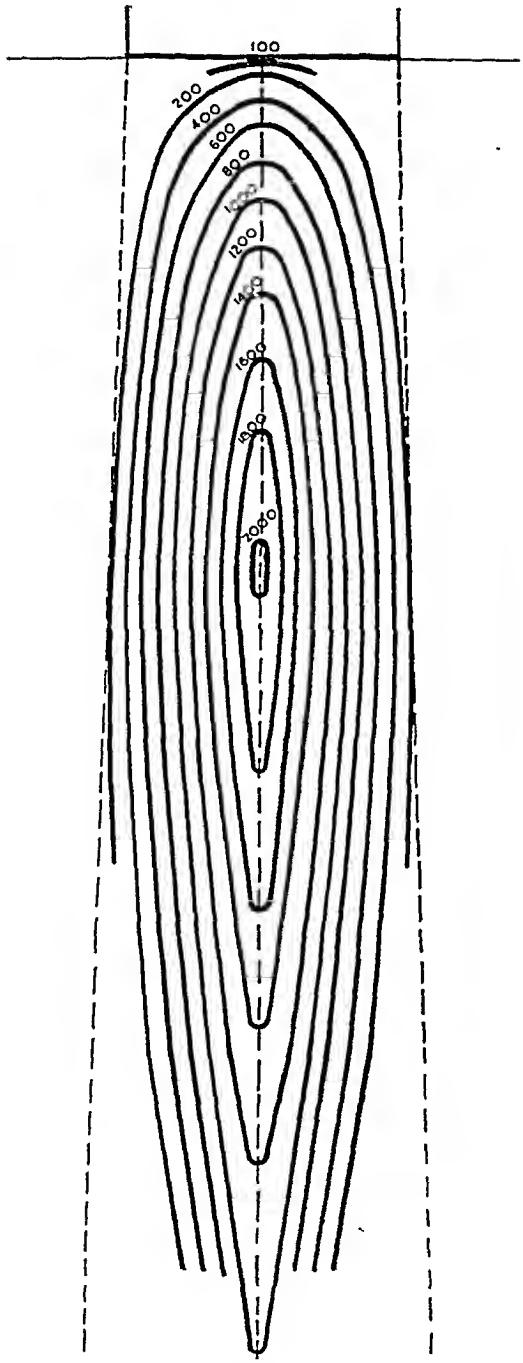



Fig. 6. 100 MeV. isodose curves. Percentage depth dose chart for a 7 cm. diameter field.

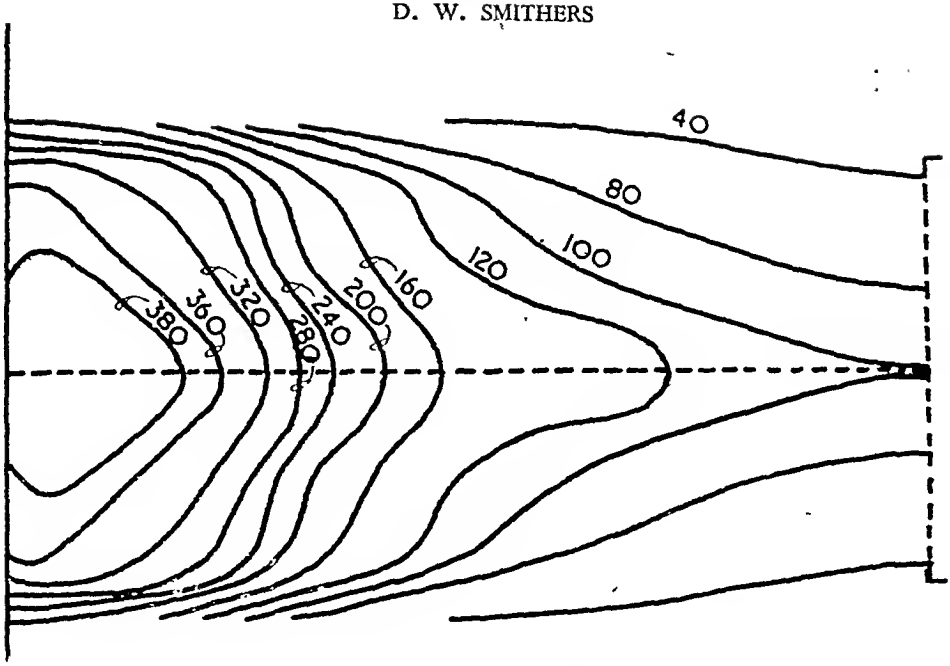



Fig. 7. Rotation distribution. 2 MeV. 100 cm., f.s.d., 7 cm. diameter circular field, represented by the dotted line on the right rotating in a horizontal plane around a circle with a 15 cm. radius.

The three dimensional distribution of the radiation is obtained by rotating this diagram about the vertical line on the left. (Adapted from a chart published by Charlton and Breed, 1948.)

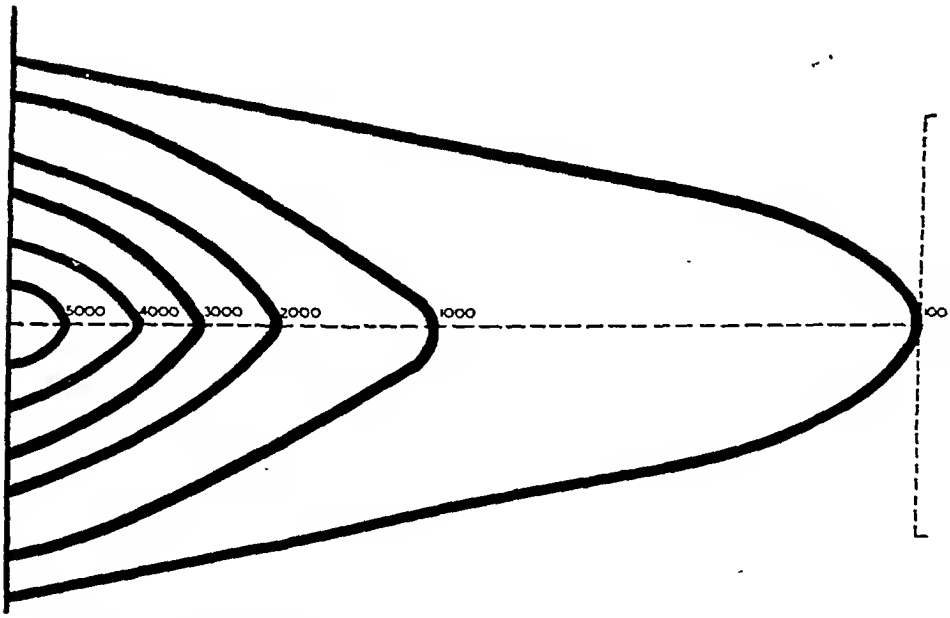



Fig. 8. Rotation distribution. 100 MeV. 132 cm., f.s.d., 7 cm. diameter circular field, represented by the dotted line on the right rotating in a horizontal plane around a circle with a 15 cm. radius.

The three dimensional distribution of the radiation is obtained by rotating this diagram about the vertical line on the left. (An estimate of the possible distribution made from the adapted isodose curves shown in Fig. 6.)

undertaken, and that clinical and biological investigations proceed together and with caution.

In the past radiotherapy has seldom achieved more, and often achieved less, with deep-seated tumours than surgery, but when this fact is seen in the light of the limited scope and slight success of surgery alone, the steady advance of radiotherapy in accessible cancer, the improvements that combinations of radiotherapy and surgery have achieved, and the new apparatus that is becoming available, renewed interest in the future of high voltage therapy for deep-seated tumours is justifiable. Without earlier diagnosis no great step forward would seem to be possible, but much more can surely be achieved than is being done at present. To the biased eyes of a radiotherapist the immediate chances of improving the prospects of patients with deep-seated cancer seem at least as likely to lie with his close co-operation with his surgical colleagues as with the discovery of some new specific cure. Whether this is so or not there can be no excuse for delaying the use of a reasonable and hopeful line of progress along established lines that is available, for the advent of some new discovery which for some of us may not come in time. Both separately and together surgeons and radiotherapists succeed in curing patients with cancer every day—whatever may be said about our occasional late recurrences. We are obtaining a better understanding of each other's problems, and arise less often in public to belittle or condemn each other's methods and more frequently to report some jointly won advance. Unfortunately, we still hear, at times, those surgeons who, on a meagre experience of inadequately treated, incurable cases sent for radiotherapy, announce that this treatment has no part to play in the attack on tumours at some site where they obtain a 5 per cent. five-year absolute survival rate. The " sent for radiotherapy " is significant. The radiotherapists who deny their patients the benefits of a surgical opinion are less numerous if no less pompous.

### The Treatment of Deep-seated Tumours in the Future

Let us examine the prospects of mutual assistance between surgeon and radiotherapist in the treatment of patients with deep-seated tumours in the future, recognizing our natural biases, pooling our skill and experience and looking for sound general principles to guide us. Surgery is curative when the whole of the malignant growth is removed. Its hope lies in localization, its fears in dissemination, and yet nothing is so conducive to spread of the disease as unsuccessful surgical interference. This is well recognized in the surgical techniques adopted in the theatre when tumours are cut into for diagnostic purposes and is reflected in the sharp drop that occurs in survival rates between early and late cases treated by surgery alone. Except as an occasional deliberate palliative procedure, which, though it may shorten life will make it more easily bearable, partial removal of malignant tumours is bad surgery. There is no place in the curative treatment of cancer for the kind of heroics

which Lord Horder has called " the triumph of technique over reason," even though the anæsthetists and penicillin have made some remarkable mutilations possible. The essence of success is selection, the careful choice of the case for operation and then bold surgery. Radiotherapy is curative when the whole of the tumour can be adequately irradiated without undue damage to the normal tissues, either because there is sufficient difference in sensitivity between the tumour and its bed or because the radiation effect can be sufficiently concentrated. These conditions are seldom met with at a depth, but so far from there being a penalty for lack of complete success, some gain can almost always be obtained even if it is temporary and slight. When the gain is considerable the risk of dissemination by surgery may be so reduced that removal of the tumour becomes a reasonable proposition. Temporary marked regression of deep-seated tumours following irradiation with arrest of growth for a few weeks or months would seem to be sufficiently common to allow of more attempts at removal during this period than are practised now. More radical operations and greater risks of cutting close to the limits of spread would seem to be justified when the activity of tumours has been reduced.

Let us explore briefly some of the possible extensions of the combination of surgery and radiotherapy for tumours at a depth. The gastro-intestinal tract has been regarded as almost the exclusive province of the surgeon in the treatment of cancer in the past. Over 2,000 people die each year with cancer of the œsophagus, over 13,000 with cancer of the stomach, over 10,000 with cancer of the intestines, other than the rectum, and over 6,000 with cancer of the rectum. The total deaths from cancer of these sites in 1945 were 32,772. With the œsophagus radiotherapy has done better than surgery, but radical surgery for these tumours has advanced rapidly of late, and it would seem to be a reasonable plan to treat all operable lower third tumours by surgery, since this is the region least amenable to radiotherapy, and most suitable for excision. For tumours of the upper two-thirds, multiple field or rotation high-voltage therapy with beams of radiation of greater penetration than have yet been available seems to offer the best prospects for the patient at present. It would be interesting to see whether pre-operative irradiation was of benefit to some of the patients with lower third tumours ; so far only one of the patients irradiated by us has been treated in this way, and he was both unusual and unfortunate. This was a man of 52, with a highly cellular adenocarcinoma of the lower end of the œsophagus, whose dysphagia was relieved following X-ray treatment in July, 1945, but who later developed pain and localized constriction of the lumen. Œsophagoscopy showed a smooth constriction 40 cm. from the incisor teeth in October, and in December he was operated on and the lower end of the œsophagus resected. The patient died two days after the operation, and serial sections revealed no evidence of residual tumour cells in the fibrous constriction at the site of the original tumour and no evidence

of any metastases could be found on post-mortem examination. No patient of ours with a new growth in this situation has remained free from recurrence after X-ray therapy for more than two years, so that the assumption that this patient had residual growth was not unreasonable, and in view of the marked improvement in his general condition and the onset of pain the indications for post-irradiation removal seemed to be sound.

The abdomino-thoracic approach has enhanced the prospects of surgery for carcinoma of the stomach. Radiotherapy has so far had little to offer. There would, however, seem to be some possibilities in the administration of irradiation to inoperable cases followed by an attempt at gastrectomy later. Some cases of good temporary regression have been noted, with radon seed implants for carcinoma of the stomach by some of my surgical colleagues at the Royal Cancer Hospital. One of these patients, a man of 57 with pernicious anæmia, developed a carcinoma of the stomach in 1946, and came to hospital in March, 1947. He was found to have an extensive gastric tumour spreading to involve the lesser omentum, liver and peritoneal surface of the stomach, and radon seeds were implanted. He gained two stone in weight, but in July, 1948, a barium meal examination showed evidence of recurrence and in September an abdomino-thoracic œsophago-gastrectomy with splenectomy and removal of the left lobe of the liver was performed successfully by Mr. Ledlie. Post-irradiation removal of an advanced carcinoma of the stomach has now been tried, and further attempts both following radon implantation and external irradiation will be made. For the moment radiotherapy would seem to have little to offer patients with tumours of the intestine, but the time has surely come to review the results of abdomino-perineal resection of the rectum once more with regard to site, form, differentiation and degree of spread in relation to the possibilities of pre-operative irradiation. There have already been some indications that radiotherapy may well improve the results that can be obtained in this situation.

With the lung, surgery has already much to its credit, but the death rate rises—7,553 in 1945. The palliative value of radiotherapy is established; even the occasional long survival is accepted as not merely a doubtful curiosity. An increase in the operability rate might well be achieved by pre-operative irradiation here. We have had one such case so far at our joint consultation clinic at the Brompton Hospital. This man of 45, with a nodular tumour of the right upper lobe bronchus and sub-carinal widening, was treated by X-rays in November, 1947. In February, 1948, he was well, and no residual tumour was visible bronchoscopically, though some distortion of the carina still remained. In March Mr. Price Thomas performed a pneumonectomy, and the remaining fibrotic squamous-cell tumour mass was removed. A trial of post-irradiation pneumonectomy has also been started, and the first patient is still feeling very well one year later.

The next commonest cause of death from cancer is carcinoma of the breast—7,359 in 1945. These are not really deep-seated tumours, but they have justified the use of pre-operative irradiation in the more advanced cases, and demonstrated the diminution in the risk of dissemination that occurs. Next in frequency as a cause of death is carcinoma of the uterus, causing 4,370 deaths in 1945. Here access provided by the vagina and cervical canal has permitted intra-cavitary treatment and favoured radiotherapy, so that now it even provides a satisfactory alternative to surgery for carcinoma of the fundus (Heyman, 1947), and is the method of choice for nearly all early cases of carcinoma of the cervix. The question as to whether radiotherapy can deal adequately with involved lymph nodes on the pelvic wall is, however, still perhaps not answered satisfactorily. Carefully planned techniques have permitted a more favourable distribution of the radiation, and high voltage X-ray therapy may help further. It would be interesting to see what effects are produced by these methods, and operation following such irradiation in a selected series of cases might show a more favourable response than has been found in the past.

These few examples will serve as illustrations of some of the possibilities for pre-operative irradiation at the more common tumour sites; several others, such as the kidney, for instance, warrant consideration in this light. Changes in outlook on the time-dose relationship and super voltage apparatus may enable us to produce permanent regression of deep-seated tumours more frequently by means of radiation alone. It seems probable, however, that even with the introduction of this higher voltage apparatus the future of X-ray therapy for deep-seated tumours will lie largely in the pre-operative field. The majority of the tumours concerned are not so sensitive to radiation that we may expect to eradicate a high proportion of them when irradiated in the midst of normal tissue.

Progress in radiotherapy in this field would, therefore, seem to depend even more than it does in others on the co-operation of surgeons. The joint consultation clinic and follow-up, the visits of radiotherapists to the theatre, and of surgeons to radiotherapy departments all help to make that progress possible. In part at least the future of high voltage X-rays in the treatment of malignant tumours at a depth depends on the attitude of surgeons to the treatment of all patients with cancer at each site and not only of those that they consider to be operable.

## REFERENCES

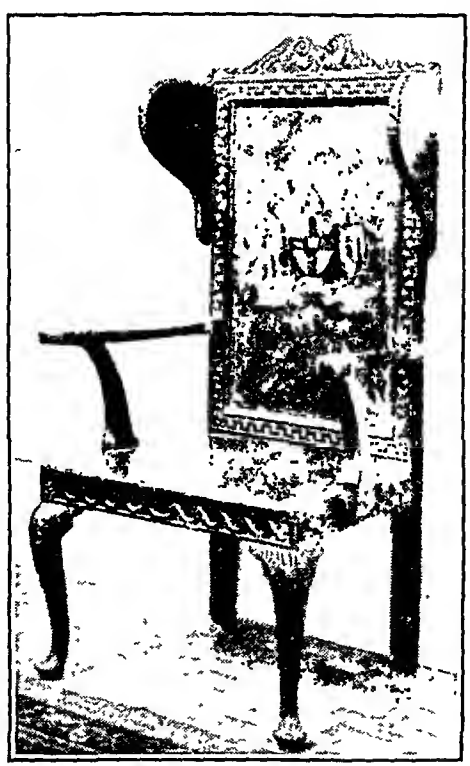
ADAMS, G. E., *et al.* (1948) *Amer. J. Roentgenol.* **60**, 153.
CHARLTON, E. E., and BREED, H. E. (1948) *Amer. J. Roentgenol.* **60**, 158.
HEYMAN, J. (1947) *Brit. J. Radiol.* **20**, 85.
MACKENZIE, S. (1939) *Rep. Publ. Hlth. Med. Subj. Lond., No.* 89.
TAYLOR, H. (1948) *Lancet*, **1**, 581.

## 16. THE ARMS OF THE COMPANY AND COLLEGE

In 1492 King Henry VII made an informal grant of Arms to the fraternity of Surgeons—a banner bearing a rose surmounted by a royal crown, the stalk being a probe or spatula.

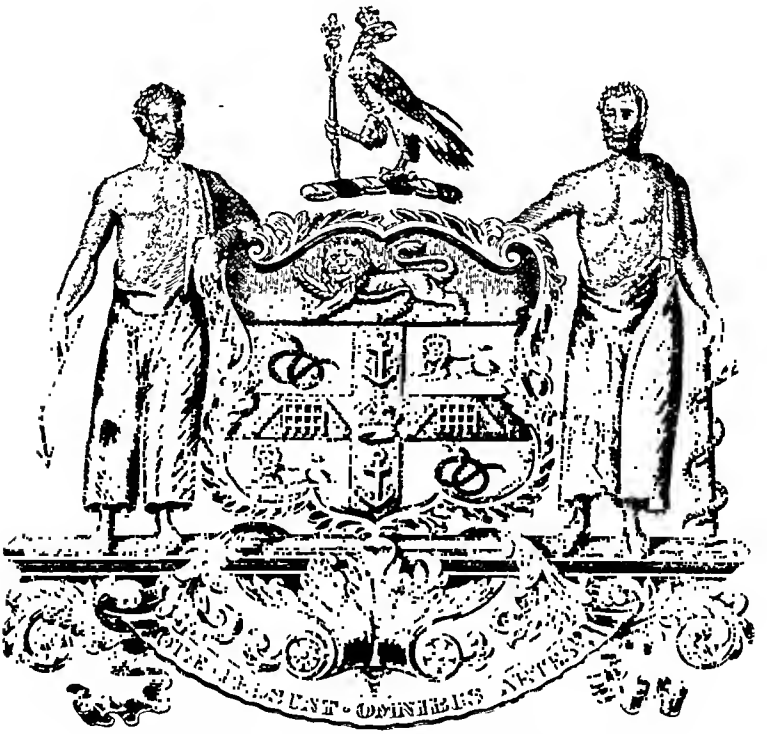
The early accounts of the Company or Corporation of Surgeons show that on 10th September, 1745, a fee of 3s. 6d. was paid for "searching for the ancient arms of the Company." This search would presumably have shown that the device authorized by Henry VII had been incorporated in the Arms of the Barber-Surgeons, when the two companies were united by Henry VIII, and that as these same Arms were retained by the Barber's Company on the separation in 1745, the Surgeons must adopt different emblems for their new Arms.

This they had apparently done before the payment of the search fee, for on 22nd August, 1745, one Mr. Brookshead was paid three guineas "for painting of Company's Arms." There are but few extant representations of the Arms assumed without licence by the Company, but they are engraved on the Ranby Cup (described in the *Annals* for March, 1948), and were depicted in colour on the Master's Chair, of which the College was dispossessed by enemy action in 1941.



The Master's Chair.

Arms of the Company of Surgeons, assumed 1745.

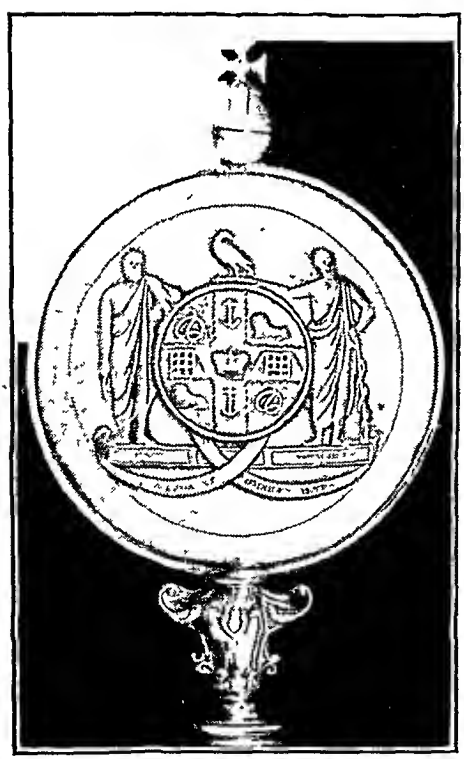


Arms of the Royal College of Surgeons, granted 1822.

It is strange that there is no minute recording the adoption of Arms by the Company of Surgeons.

The quartering was the same as in the present Arms of the College—green serpents entwined on a gold field in the first and fourth, lions " proper " couchant on a silver field in the second and third. The cross was blue and ingrailed, but the emblems placed thereon were, as now, a crown in the centre, two portcullises in fesse and two anchors in pale, all golden. The crest was an eagle, in natural colours, and the present motto was used—Quæ prosunt omnibus artes (the Arts which are of service to all). The supporters were the brothers Machaon and Podalirius, surgeons to the Greek forces at the siege of Troy, the former holding the broken arrow which he extracted from the side of King Menelaus. An article dealing with the Supporters appeared in the *Annals* for December, 1948.

The Royal College of Surgeons, when incorporated in 1800, continued to use the same Arms, but by 1802 Podalirius was holding the staff of Æsculapius, his father. This is illustrated on the Bedell's Staff (hall-marked 1803-4) which was used by the College before the grant of a mace, and which now stands in the Entrance Hall.



The Bedell's Staff of the Royal College of Surgeons.

The Staff is still used as an emblem of authority when the Mace is in use elsewhere in the College.

In 1822 the College obtained a formal grant of the Arms which it still uses. The new design was to a great extent a confirmation of the old, but a Cross of St. George was substituted for the blue ingrailed cross, and three especial marks of honour were added—a lion (gold on a red field) " in chief," being part of the Arms of England, an Imperial crown in place of the regal crown on the cross, and another Imperial crown surmounting the crest. The eagle was also given a mace to hold in its dexter claw, representing the mace presented to the College at that time by King George IV.

There seems to be no record of the intended significance of the earlier symbols, but lions couchant in heraldry should be emblematic of sovereignty, and serpents of wisdom or subtilty. There is a tradition in the College that the anchors refer to the function of examining Naval Surgeons, enjoined on the Barber-Surgeons by Charter in 1629, and perhaps the portcullises have a military significance and represent a similar duty in respect of Surgeons to the Army entrusted to the Corporation in 1745.

By a strange coincidence these symbols, assumed when the Corporation of Surgeons had its Hall at the Old Bailey, are especially appropriate to the present site of the College, an anchor being the badge of the parish of St. Clement Danes and the portcullis having a prominent place in the Arms of the City of Westminster.

K.C.

## THE RESTORATION AND DEVELOPMENT FUND

SINCE THE REPORT in the March number of the *Annals* several generous gifts have been received, notable among which are the following: Mr. R. K. Bowes has given a further donation bringing his contribution up to one hundred and ten guineas; one hundred guineas from O. J. Vaughan-Jackson, George Seed, L. P. Le Quesne, Henry Hamilton Stewart and J. C. Ogg: seventy pounds from F. Noel Glover and G. K. Rose; and fifty guineas from W. E. Barnie-Adshead and E. Mervyn Evans.

Several Fellows of the College have given smaller donations and these are doubly appreciated for in a campaign like this it is numbers that count as well as amounts as evidence of loyal attachment to the College.

The total is now over £194,000. £2,250 has been subscribed by Fellows of the College since the last appeal letter from the President on February 14 this year.

# THE LIBRARY

## VESALIUS AND LISTER

### TWO NOTABLE ACQUISITIONS

---

A VERY NOTABLE addition has been made to the College's collection of books by Vesalius, which are the master works of graphic anatomy. A rare opportunity has been taken to buy a copy of his *Epitome*, published at the same time as his great treatise, the *Fabrica*.

This rare volume is a tall atlas of wood-engravings, larger than those in the *Fabrica* and designed as diagrams for teaching. Because of this practical use and its unhandy size, the book is much rarer than the *Fabrica*; only four copies are recorded in Britain.

Vesalius published three great anatomical books. First, to indicate how he intended to reform the presentation of diagrams for those watching dissections, he issued at Venice in 1538, when he was 23, six very large engravings known as the Six Tables (*Tabulae sex*); two complete sets alone survive. The College possesses a copy of the rare nineteenth-century facsimile.

Secondly, in June 1543, Vesalius published his masterpiece *De humani corporis fabrica libri septem*, one of the most beautiful books ever printed, which has had a profound influence on scientific thought and method. This great book, a folio of nearly 700 pages, is a typical product of the High Renaissance in its marriage of science and art. It sets out in detail and with a wealth of illustrations a complete survey of human anatomy.

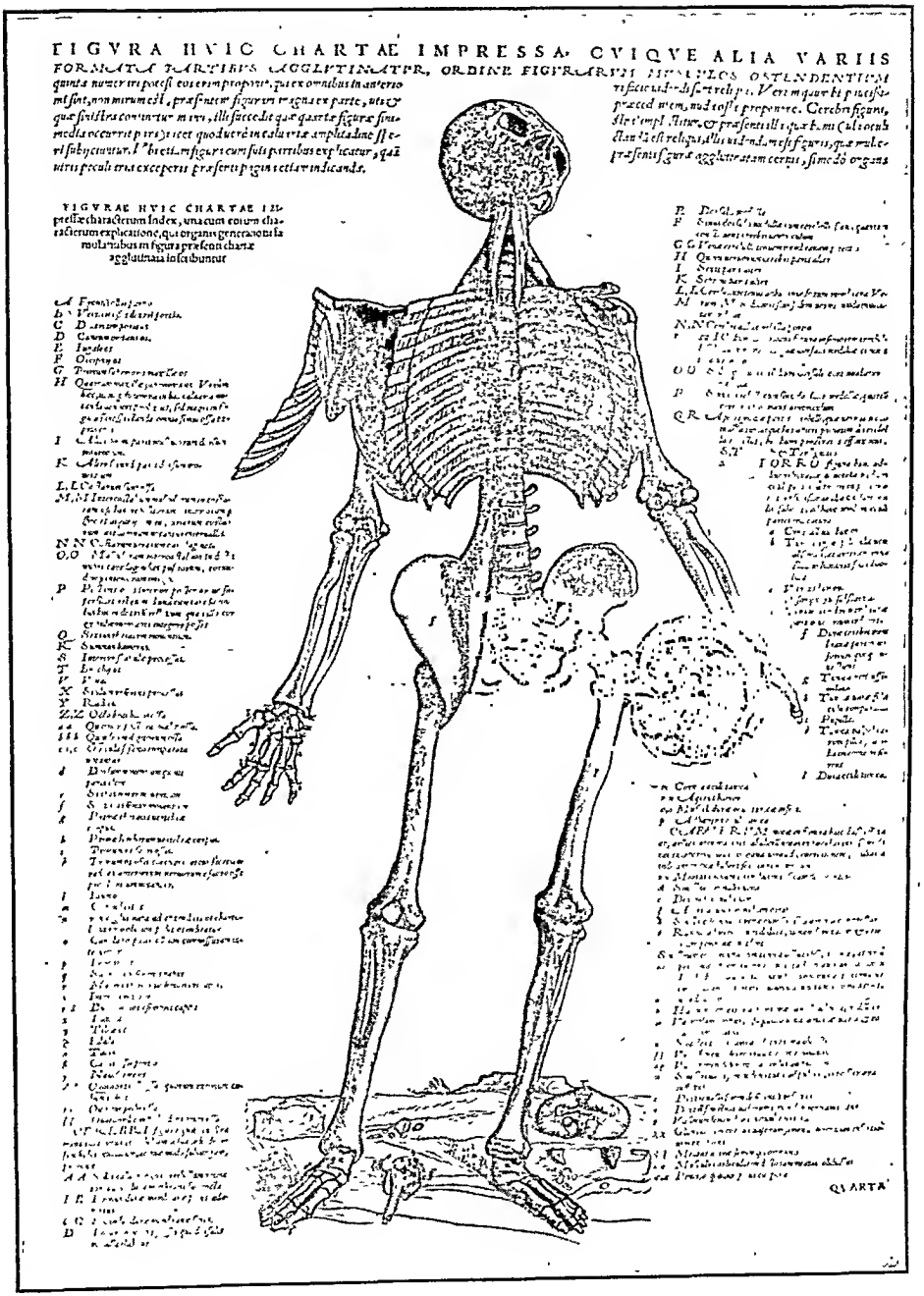
At the same time Vesalius knew that a simpler medium was needed to make his new teaching available in practical study. So he made ready for simultaneous publication a third series of woodcuts, larger than those of the *Fabrica*, with an *Epitome* of its seven books in six short chapters. They form a splendid book, and its acquisition provides a chief glory to the Library.

The nine plates of the *Epitome* form a sequence showing five layers of muscles from the deepest upwards, a skeleton, a magnificent pair of naked figures, male and female, and a chart of the brain and nerves. Apparently as an afterthought the plate of the nervous system was also used, folded, in the *Fabrica*, with a similar folded plate of the blood vessels, evidently designed for the *Epitome*.

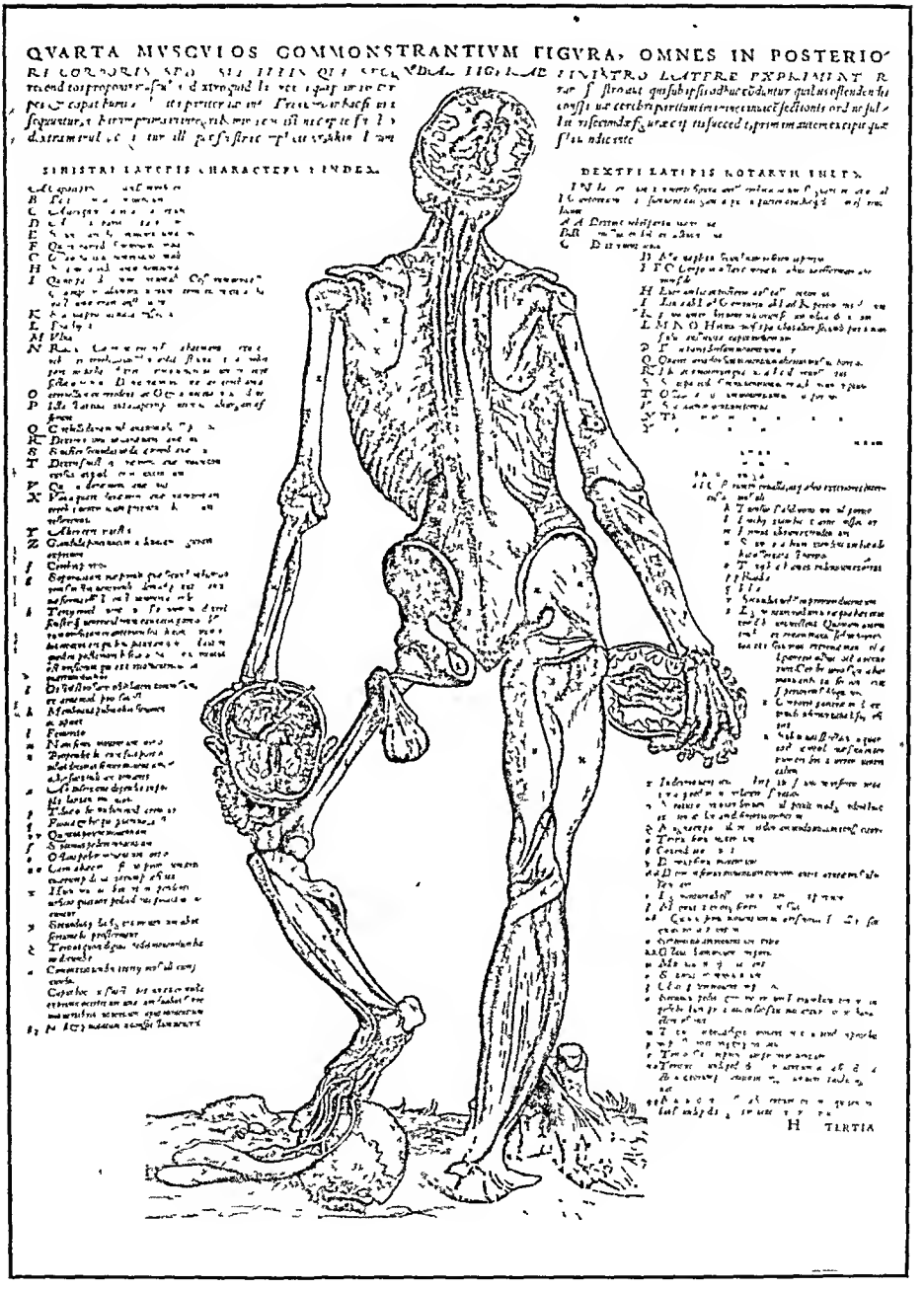
---

### *Lister's move from Edinburgh to London*

Lister came to London in 1877 in order to spread the knowledge of antisepsis himself where it had received least attention. He gave up a leading position at Edinburgh and accepted a comparatively minor post. On the death of Sir William Fergusson someone at King's College




VESALIUS EPITOME 1543.
Fifth plate of the muscles.




VESALIUS EPITOME 1543.
Fourth plate of the muscles.

Hospital, probably Sir William Bowman, suggested that Lister should be brought south as professor of systematic surgery, when John Wood was promoted to Fergusson's clinical chair. Lister let it be known that he would come on his own terms, which involved some concession by Wood; and at what he believed to be a private meeting he criticised the teaching methods in London. His speech was reported, and roused indignation, especially as he had not been officially invited to London. Delicate negotiations continued, but after much controversy the Council of King's College created a second chair of clinical surgery and elected Lister to it on June 18, 1877.

The Library has lately acquired an autograph letter from Lister, which exhibits his hopes and motives clearly. It adds a valuable personal touch to the story told by Godlee in his life of *Lord Lister* (1917) and by Mr. H. Willoughby Lyle in his *King's and some King's men* (1935):

8 Charlotte Square
Edinburgh
*8th March* /77

My dear Dr. Murray

I am very much obliged to you for your kind and cordial letter. My position here is really all that man can well desire. But I should be willing to accept an invitation to King's, if arrangements in all respects satisfactory could be made to enable me to carry out the two objects which I should in reality have in view, *viz.*, the thorough working of the antiseptic system with a view to its diffusion in the metropolis and the introduction of a more efficient method of clinical surgical teaching than has hitherto prevailed in London. I should not care about the rank I held in the smallest degree, but I should consider it essential that I should be allowed to give a regular course of clinical lectures in the operating theatre twice a week, to be on the same footing as other college courses, and that I should not be required to deliver systematic lectures.

But I am already in communication with some members of the staff of King's; and unless those who have spoken to you are in your opinion likely to be independently influential either with Mr. Wood or with members of the Council, it would perhaps be needless for me to enter more fully at present into the conditions on which I would go. I will merely add that, as Mr. Wood would rank as Senior Surgeon, and as there is nothing in the nature of things to make the clinical chair higher in dignity than the systematic, I do not see that Mr. Wood need feel aggrieved by the proposed arrangement. Thus at University College Mr. Marshall is Senior Surgeon and yet prefers the position of giving the Systematic lectures. The mere fact of Fergusson having held the clinical chair is surely a matter of no great moment; more especially as I should propose to hold the office not in a merely nominal manner as Sir William did, but as a place of downright hard work. Believe me, My dear Dr. Murray,

Very sincerely yours
JOSEPH LISTER

## MONTHLY DINNERS

Monthly dinners are held in the College on the second Wednesday of each month. The following are entitled to attend with their guests : All Diplomates and students of the College, and Members of the Associations linked to the College through the Joint Secretariat. It is not necessarily intended that guests should be members of the medical profession.

The dinners will be at 7 p.m. on the following Wednesdays : May 11, June 8, and July 13, 1949. There is an inclusive charge of £1 5s. (including drinks), which must be sent with the application to the Assistant Secretary at least a week before the date of the dinner. The dress is Lounge Suit or Uniform.

---

## DIARY FOR APRIL (19th-29th)

| | | |
|---|---|---|
| Tues. 19 | | Last day for nomination of candidates for the Council. |
| | 5.00 | MR. T. TWISTINGTON HIGGINS—Abdominal Surgery in Children. |
| | 6.15 | SIR HUGH CAIRNS—General Principles in Intracranial Operations. |
| Wed. 20 | 10.00 | DR. R. W. COPE—Anæsthesia for Children. |
| | 11.15 | DR. VICTOR GOLDMAN—Vinesthene. |
| | 5.00 | DR. VERNON F. HALL—Anæsthesia and Analgesia in Obstetrics. |
| | 5.00 | MR. J. B. OLDHAM—Surgery of Sacrococcygeal Region. |
| | 6.15 | MR. G. F. ROWBOTHAM—Head Injuries. |
| Thur. 21 | 10.00 | DR. VERNON F. HALL—Anæsthesia and Analgesia in Obstetrics. |
| | 11.15 | DR. PHILIP J. HELLIWELL—Refrigeration and Electronarcosis. |
| | 5.00 | DR. STANLEY ROWBOTHAM—The Relation of Endocrine Imbalance to Anæsthesia. |
| | 5.00 | MR. J. E. A. O'CONNELL—Surgical Treatment of Neuralgias. |
| | 6.15 | SIR GORDON GORDON-TAYLOR—Some Aspects of Cancer Surgery. |
| Fri. 22 | | D. Phys. Med. Examination (Part I) begins. |
| | 10.00 | DR. RONALD WOOLMER—Convulsions. |
| | 11.15 | DR. RONALD WOOLMER—Oxygen Therapy. |
| | 5.00 | DR. W. D. WYLIE—Pulmonary Complications. |
| | 5.00 | MR. E. W. RICHES—Surgery of Urinary Calculi. |
| | 6.15 | MR. RONALD MACBETH—Osteomyelitis of the Skull Bones Secondary to Sinusitis. |
| Mon. 25 | 3.45 | PROF. J. D. BOYD—Formation of and Early Changes in the Germ Layers. |
| | 5.00 | DR. H. F. BREWER—Blood Groups and Blood Grouping. |
| Tues. 26 | | Last day for applications for Lectureships. |
| | 3.45 | PROF. H. A. HARRIS—Limb Plexuses. |
| | 5.00 | DR. H. F. BREWER—Some Aspects of Blood Transfusion. |
| Wed. 27 | 3.45 | PROF. H. A. HARRIS—Inversion and Eversion of the Foot. |
| | 5.00 | PROF. H. L. SHEEHAN—The Pathology of the Pituitary. |
| Thur. 28 | 3.45 | PROF. J. H. DIBLE—Inflammation and Repair. |
| | 5.00 | PROF. C. F. M. SAINT—Stomatodæal Ruminations, Clinical and Non-Clinical. |
| Fri. 29 | | Voting papers for Council Election issued. |
| | | L.D.S. Examination (Properties of Dental Mechanics and Dental Materials) and D. Phys. Med. Examination (Part II) begin. |
| | | Last day for nomination of Candidates for Faculty of Dental Surgery Board. |
| | 3.45 | PROF. J. H. DIBLE—Inflammation and Repair. |
| | 5.00 | PROF. R. I. HARRIS—Spondylolisthesis. |

# DIARY FOR MAY

| | | |
|---|---|---|
| Mon. 2 | | L.D.S. Examination (Dental Mechanics) begins. |
| | 3.45 | PROF. J. D. BOYD—The Development of Genito-Urinary System. |
| | 5.00 | PROF. N. F. MACLAGLAN—The Plasma Proteins. |
| Tues. 3 | 3.45 | PROF. JOHN KIRK—Joints and Movements of the Vertebral Column. |
| | 5.00 | PROF. N. F. MACLAGLAN—Urinary Hormones. |
| Wed. 4 | 3.45 | MR. A. M. A. MOORE—Synovial and Tissue Spaces of the Hand. |
| | 5.00 | DR. N. H. MARTIN—The Applied Physiology of the Parathyroid. |
| Thur. 5 | | Final F.R.C.S. Examination (Ophthalmology and Otolaryngology) begins. |
| | 3.45 | MR. CLIVE BUTLER—The Anatomy of the Rectum and Anal Canal. |
| | 5.00 | DR. N. H. MARTIN—Liver Efficiency. |
| Fri. 6 | | D.A. Examination (Part I) begins. |
| | 3.45 | PROF. J. D. BOYD—Development of the Nervous System and Ectodermal Derivatives. |
| | 5.00 | PROF. GEOFFREY HADFIELD—The Lymphadenopathies. |
| Mon. 9 | | Final Fellowship Oral Examination (Ophthalmology and Otolaryngology) begins. |
| | 3.45 | PROF. J. WHILLIS—The Tongue and Soft Palate. |
| | 5.00 | DR. R. G. MACFARLANE—The Hæmorrhagic States. |
| Tues. 10 | | Final F.R.C.S. Examination (General Surgery) begins. |
| | 3.45 | PROF. J. WHILLIS—The Larynx. |
| | 5.00 | DR. R. G. MACFARLANE—The Hæmorrhagic States. |
| Wed. 11 | 3.45 | PROF. D. V. DAVIES—The Development of Joints. |
| | 5.00 | DR. A. SCHWEITZER—Problems of Cardiac Physiology. |
| | 7.00 | Monthly Dinner for Fellows, Members and Licentiates (*see page* 265). |
| Thur. 12 | 5.00 | PROF. HAMILTON BAILEY—Hunterian Lecture—Parotidectomy: Indications and Technique.* |
| Fri. 13 | | D.A. Examination (Part II) begins. |
| | 3.45 | DR. DAVID SINCLAIR—The Superior Mediastinum. |
| | 5.00 | DR. A. SCHWEITZER—Cardiovascular Reflex Regulation. |
| Mon. 16 | | Final Fellowship Oral Examination (General Surgery) begins. |
| | 3.45 | DR. F. A. FELL—Anatomy of Pronation and Supination of the Forearm. |
| | 5.00 | PROF. A. HEMINGWAY—The Control of Breathing. |
| Tues. 17 | 4.00 | SIR EDWARD MELLANBY—Jenner Oration.* |
| | 5.30 | PROF. A. HEMINGWAY—Physiology of Exercise. |
| Wed. 18 | 3.45 | DR. E. L. PATTERSON—Orbital Contents. |
| | 5.00 | DR. J. E. CATES—Renal Function. |
| Thur. 19 | 3.45 | PROF. D. V. DAVIES—Cerebral Circulation. |
| | 5.00 | DR. J. E. CATES—Renal Function. |
| Fri. 20 | | Voting papers for Faculty of Dental Surgery Board Election issued. |
| | 4.00 | PROF. THOMAS NICOL—The Kidneys, Ureters and Bladder. |
| Mon. 23 | 3.45 | PROF. F. WOOD JONES—The Muscles of the Body Wall. |
| | 5.00 | DR. A. C. CROOKE—Adrenal Hormones. |
| Tues. 24 | 3.45 | PROF. F. GOLDBY—The Facial Nerve. |
| | 5.00 | DR. W. FELDBERG—The Autonomic Nervous System. |
| Thur. 26 | 3.45 | PROF. T. B. JOHNSTON—The Tympanic Cavity. |
| | 5.00 | DR. W. FELDBERG—The Theory of Chemical Transmission of Nerve Effects. |
| Fri. 27 | 3.45 | PROF. T. B. JOHNSTON—The Anatomy of the Cerebrospinal Fluid. |
| | 5.00 | DR. C. C. N. VASS—Digestion. |
| Mon. 30 | 3.45 | DR. C. HOWARD TONGE—Lymphatic Drainage of the Head and Neck. |
| | 5.00 | DR. C. C. N. VASS—Digestion. |
| Tues. 31 | 3.45 | PROF. JOHN KIRK—Autonomic Innervation of the Head and Neck. |
| | 5.00 | PROF. A. C. FRAZER—Fat Absorption and Metabolism. |

*Not part of courses.

# THE LIFE AND ACHIEVEMENTS OF JOSEPH THOMAS CLOVER

The Joseph Clover Lecture delivered at the Royal College of Surgeons
on
16th March, 1949
by

A. D. Marston, F.R.C.S., F.F.A.R.C.S.
Dean, Faculty of Anæsthetists, Royal College of Surgeons

IN THIS FIRST Joseph Clover memorial lecture I shall endeavour to give a concise description of the life and scientific achievements of Joseph Thomas Clover, and this pleasant duty has been much assisted by the kindness and generosity of Dr. Martin Clover, Miss Mary Clover, and by my old friend and colleague Professor Macintosh.

As you may know Joseph Clover neither wrote a text book on anæsthesia nor did he publish many scientific papers, but he had in his possession a considerable store of notes, sketches and experimental models which were presented to the Department of Anæsthetics of the University of Oxford in 1939 by two of his surviving children, Miss Mary Clover and Dr. Martin Clover. I have been given the privilege of examining these and have secured much valuable information.

Joseph Clover was born on February 28, 1825, in the town of Aylesham in Norfolk, a county in which members of the Clover family had long been established. They were descended from sound Yeoman stock, and here is a brief genealogical tree drawn up by Miss Clover :

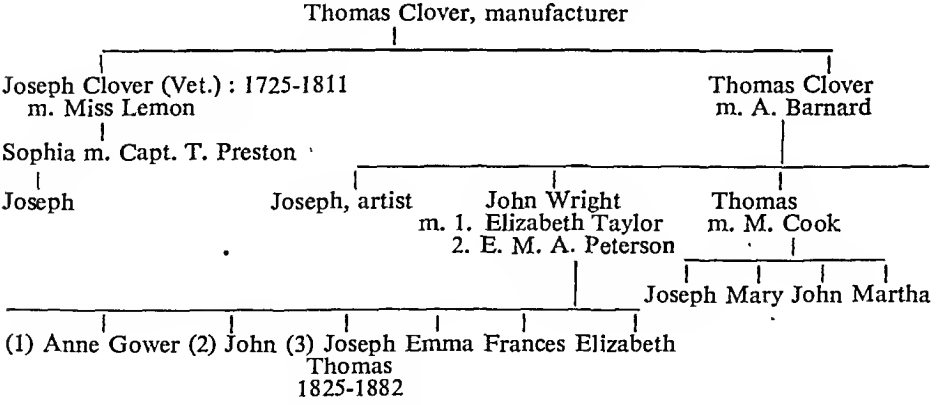



Fig. 1. The Clover Family Tree.

In regard to Joseph Clover, the great uncle of Joseph Thomas Clover, Sir Buckston Browne remarked in an address given to the section of Anæsthetics of the Royal Society of Medicine on March 7, 1913 :

"On turning to the *Dictionary of National Biography* I find that Clover's great uncle, the distinguished veterinary surgeon of Norwich, who

flourished from 1725 to 1811, is judged worthy by the editor, the late Sir Leslie Stephen, of half a column of notice. This great uncle devoted his life to veterinary science; he invented an apparatus for the cure of broken tendons and bones in horses, and in 1753 he became the discoverer of the manner in which larvæ of bots are conveyed from the coat of a horse into its stomach. We have thus a very interesting example of qualities appearing in one generation after another in the same family, for the Clover of whom we speak tonight was in his very essence a creator, an inventor, and this quality of mechanical invention deserves, I think, to be called genius, for fundamentally genius means the begetting, the creating faculty."

Clover's uncle Joseph was a distinguished artist, and he painted an excellent likeness of his nephew as a young man which is reproduced here by kind permission of Dr. Martin Clover.

Fig. 2. Joseph Clover in 1844, painted by his uncle.

Miss Clover informs us that the first marriage of her grandfather to Elizabeth Taylor was a genuine romance, as the ceremony took place at Gretna Green. John Wright Clover subsequently married Miss E. M. A. Peterson and of their six children, Joseph Thomas Clover was the third child.

Clover was educated at the Grey Friars Priory School at Norwich, and here is an illustration of one of his copy books in 1838. Master J. T. Clover was 13 years old at the time.

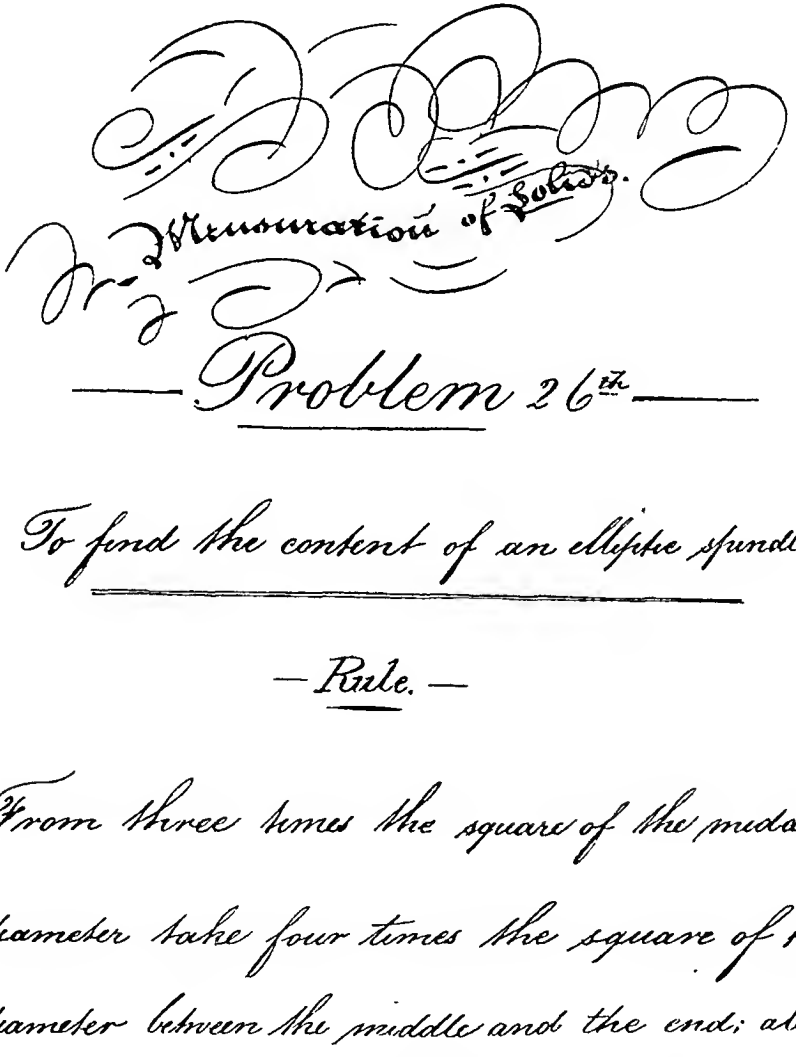



Fig. 3. Joseph Clover's handwriting at the age of 13.

After leaving the Priory School Clover was apprenticed to Mr. Gibson of Norwich and in 1842 became a dresser at the Norfolk and Norwich Hospital, a post he held until 1844 when, at the age of 19 years, he proceeded to University College Hospital.

On Monday, December 21, 1846, the first administration in Europe of a general anæsthetic for a surgical operation was carried out at University College Hospital. In a leading article published in the *Lancet* on March 29, 1913, we read: "During his stay at University College, London, and University College Hospital he was amidst the inception of great happenings. With Lister as a fellow student, with the advent of anæsthesia, and with the inspiration of such men as Liston and Syme, a keen neophyte like Clover might well 'dream dreams and see visions.' We do not know whether either Joseph Lister or Joseph Clover was present in 1846 when Liston performed his first surgical operation upon a patient under ether."

So great an occasion could hardly have been without an impelling force for Clover was always eager to see whatever was new in order that he might, if possible, improve upon it.

Similar doubts as to Clover's presence on this great occasion have been expressed by other writers, but on reading Clover's lecture notes, I discovered the following passage which puts the matter beyond any doubt:

"I was a junior student at University College when Ether was first used there and saw Liston amputate a man's thigh under its influence. I was also present when the same surgeon brought some chloroform and gave it by means of a glass breast pump. The chloroform took the place of ether immediately, and until the fatal case occurred in the practice of Sir John Fife of Newcastle we were unanimous in preferring chloroform."

As a student Clover showed a great aptitude for clinical work and in due course became house surgeon to Morton and in 1848 to Syme, after which he was appointed Resident Medical Officer and held this position for five years. Clover administered many anæsthetics as Resident Medical Officer and his work is mentioned in John Snow's historic text-book "On Chloroform and Other Anæsthetics" published in 1858(1).

In discussing the details of a fatal case at University College Hospital in 1854, Snow writes: "This plan of administering chloroform with the head and shoulders of the patient covered with a towel, was introduced by Mr. Clover, who was for several years a resident officer of the institution; and it is but right to state that it lead to no accident in his hands; in those of his successors it was, however, less successful; three accidents having occurred in a little more than a year and a half."

Clover passed his final F.R.C.S. examination in 1850, and in 1853 commenced private practice at 3, Cavendish Place at the age of 28 years. For about five years Clover practised partly as a general practitioner

and also as an anæsthetist, but two factors probably influenced him in becoming almost entirely an anæsthetist. The first was his delicate constitution which rendered him unsuited for the arduous duties of general practice, and the second was the sudden death of John Snow in 1858.

After this event, Clover proceeded to specialise almost entirely in anæsthesia, and was appointed Lecturer in Anæsthetics to University College Hospital, Chloroformist to the Westminster Hospital, and Administrator of Anæsthetics to the London Dental Hospital.

Clover developed a great interest in, and enthusiasm for, the creation of improved techniques for the administration of anæsthesia, and he proceeded to fit out a work-room at his residence with benches, tools and lathes, and spent much of his spare time in perfecting the various forms of original apparatus which he invented. Clover's first great contribution was the introduction of a chloroform bag inhaler, which enabled induction and maintenance of anæsthesia to be carried out by the inhalation of a mixture of air containing a definite proportion of chloroform.

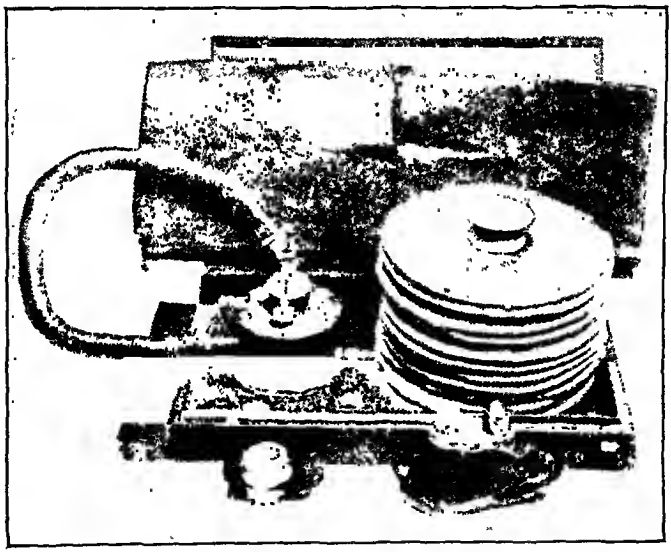
John Snow had first tried this plan in 1849 and in his book "On Chloroform and Other Anæsthetics" writes: "The most exact way in which it is practicable to exhibit chloroform to a patient is to introduce a measured quantity into a bag or balloon of known size and then to fill it up by means of bellows, and allow the patient to inhale from it, the expired air being prevented from returning into the balloon by one of the valves of the facepiece to which it was attached." Snow noted that patients were easily and comfortably induced with a mixture of 4 per cent. of chloroform in air, but remarked: "I did not try, however, to introduce this plan into general use, as the balloon would sometimes have been in the way of the surgeon, and filling it with the bellows would have occasioned a little trouble." Clover overcame this difficulty by inventing a bag which could easily be suspended over the back of the administrator and which contained a 4 per cent. mixture of chloroform in air.

In regard to the construction of the bag, Clover writes: "The bag was for a long time a difficulty with me. All the ordinary airproof materials, if sufficiently flexible, are acted upon by the chloroform vapour. I tried many ways of lining the bag to defend it from and enable it to retain the chloroform, and found the best material to be the thinnest silk waterproof cloth called siphonia, varnished with a mixture of glue and treacle, and then covered with the thinnest tissue-paper. The object of the paper is to prevent the opposite sides of the bag adhering when it is folded up."

Clover invented an ingenious apparatus for charging the bag, and this consisted of a portable bellows containing 1,000 cubic inches of air and this was blown across an evaporating vessel into the bag. Here is an illustration of the "vessel" which enables a measured dose of chloroform to be mixed with air, so that 100 inches of air contained $3\frac{3}{4}$ cubic inches of chloroform vapour.

*By kind permission of the Nuffield Department of Anæsthetics, Oxford.*

Fig. 4. Joseph Clover demonstrating how chloroform was administered with his apparatus.
(From the original photograph, presented by his daughter, Miss Mary Clover, to the Nuffield Department of Anæsthetics, Oxford.)



*Original in the Wellcome Historical Medical Museum, by permission.*

Fig. 5. Clover's chloroform apparatus packed into a small box and was readily transportable.

The chloroform bag was connected to the facepiece by a flexible tube, three feet in length. The facepiece was composed of flexible metal and lined with rubber so as to accurately fit the face. The facepiece contained an inspiratory and an expiratory valve, and they were most efficient in action. Clover said : " The valves in the facepiece are thin discs of ivory or vulcanite, made to move in one plane by means of a spindle passing through them, and supported by a spiral spring of fine wire. They act equally well in whatever position the patient's head may be, and the chloroform does not render them inefficient, as it does the flaps of india-rubber." The facepiece also contained a sliding door to admit additional air and so reduce the concentration to a percentage lower than 4 per cent.

In using the apparatus Clover commenced induction with a 2 per cent. mixture and gradually increased the strength of the vapour so as to secure induction of anæsthesia in from five to seven minutes.

This apparatus was described by Clover in 1862, and exhibited at the International Exhibition held in London in that year.

In a paper read before the Odontological Society of Great Britain in 1868 on the Administration of Chloroform in Dental Operations, Clover stated that he had used this apparatus on 1,802 cases " not only without any fatal results, but with uniform success, in the induction of complete anæsthesia." It is of interest to relate that Clover used this apparatus for the anæsthetic administered to H.M. Queen Alexandra, when Princess of Wales, for an operation on the knee.

Although Clover administered chloroform so successfully and safely in the early 'sixties, this drug was proving increasingly dangerous in the hands of less skilled administrators.

Mrs. Duncum remarks in her valuable book(2) that by 1863, 123 fatal cases had been recorded, and the medical profession was becoming increasingly disturbed by these fatalities which often occurred during the performance of trivial or minor surgical operations. This led to the formation in 1864 of a committee by the Royal Medical and Chirurgical Society, and although not an actual member, Joseph Clover was co-opted to attend meetings, and in fact carried out most of the experimental work on small animals, using his chloroform apparatus, which he ingeniously modified for this purpose. As is well known, the findings of the committee stated the fact that ether was a much safer and quite as efficient an anæsthetic as chloroform, but it suffered from the disability of rarely providing a smooth and efficient induction because of its irritant qualities. And so the committee advised the use of chloroform mixtures, but Clover was not favourably impressed by their safety or value, and resolutely commenced his long but successful search for a method in which ether could be used efficiently and safely, so that the routine use of chloroform could be discontinued.

In this endeavour he was assisted by the events which occurred in 1868 and 1869.

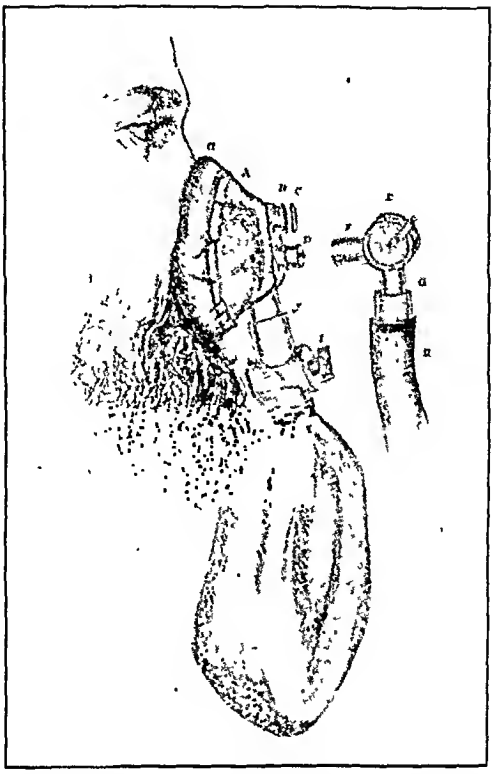
After the tragic failure of the demonstration by Horace Wells of nitrous oxide at the Massachusetts General Hospital in 1845, this useful anæsthetic agent was not employed for many years. Its use was revived by Colton in 1862 and this time with success, for by 1867 Colton had records of no fewer than 24,000 cases in his clinic at New York.

At this time Colton visited Paris to attend the international exhibition and the First International Medical Congress. Whilst in Paris he met Dr. T. W. Evans, a fellow-countryman who had practised in the French capital as a dental surgeon for a number of years, and instructed him how to prepare and administer nitrous oxide gas. Evans proved an apt and enthusiastic pupil and used this agent for the extraction of teeth with great success. In March, 1868, Evans came to London and gave several demonstrations at the National Dental Hospital. Clover was present and records his impressions in the excellent paper which he delivered before the annual meeting of the British Medical Association held at Oxford in August, 1868.

Clover remarked upon the cyanosis, muscular spasm and imperfect narcosis observed in some of the administrations. But on the whole Clover was impressed by the general efficiency of the anæsthesia attained, and he immediately commenced to improve the somewhat primitive character of the apparatus. Alfred Coleman in his text-book published in 1881(3) remarks: "Our readers, acquainted with the present modes and appliances for administering nitrous oxide, would smile at the cumbrous and rough apparatus at first employed. A large india-rubber bag or balloon contained the gas, connected by a long tube to a wooden mouthpiece with inlet and outlet valves. The mouthpiece was placed between the patient's teeth, and the lips compressed over it with the fingers, whilst the finger and thumb of a bystander unceremoniously closed the patient's nostrils."

In his paper read at Oxford in August, 1868, Clover remarks, "As I witnessed these cases of Dr. Evans, and as my chloroform apparatus was well fitted to serve for giving nitrous oxide, I lost no time in commencing to administer it, in a few cases it answered very well, in others—such as those who had thin cheeks which were drawn in during inspiration—and those who had much hair on the face, the results were often unsatisfactory. The facepiece was made larger and very carefully fitted, but yet the patient would sometimes draw air under it. As this appeared to me to arise from the gas not being able to travel quickly enough along the tube during the forced movements of respiration, I added a supplemental bag holding about 200 inches connecting it with the facepiece by means of a tube in which there was a stopcock."

In due course, as Sir Frederic Hewitt informs us in his text-book published in 1893(4) Clover discovered that: "He could get all the advantages of his 'supplemental bag' by dispensing altogether with an inspiratory valve in the facepiece," in which case it was necessary to be sure that the supply bag was kept constantly full so that the expiratory valve would



*From Duncum's Development of Inhalation Anæsthesia.*

Fig. 6. Clover's rebreathing bag, called by him the "Supplemental Bag," for nitrous oxide administration (1868). The type of facepiece and the stopcock also devised by Clover are shown.

"The woodcut represents the facepiece applied, with the supplemental bag M attached. A. Soft pad of india-rubber. C. The valve opening during expiration. D. The mount upon which the stopcock, F, G, fits; the spindle part of the inspiring-valve is seen projecting. E. Opening in the stopcock of inhaling tube, which permits air to be breathed whilst the face piece is adjusted. When the little knob is turned down to G, the opening, E, is closed, and the supply tube, H, leading from the bag of gas, is opened. M. The supplemental bag to be used or not by turning the stopcock, L."

function. Hewitt also remarked: "The bag may at any moment be made to play the part of the 'supplemental bag' by stopping the supply of fresh nitrous oxide and placing the thumb over the expiratory valve." Fig. 6 shows Clover's "Supplemental Bag."

In 1869 we find Clover improving his nitrous oxide apparatus and still endeavouring to discover a method of administering ether satisfactorily, but another interest was now to have a beneficial effect upon his career. Clover had now resided at 3, Cavendish Place for 16 years and at the age of 44 was still a bachelor.

During these 16 years Clover had achieved many of his ambitions, and he was increasingly regarded as the leader of the new specialty of anæsthetics, but his life must have been somewhat lonely, and the news of his engagement to Miss Mary Anne Hall, the daughter of the Rev. T. G. Hall, Prebendary of St. Paul's Cathedral, was received with great satisfaction by his relatives and numerous friends. The marriage took place

on November 2, 1869, at St. Margaret's, Westminster, and Clover during his remaining years received from his wife great inspiration and assistance in his work. Five children were born, the eldest—a boy—died in childhood ; of the others two sons, and the daughter, still survive. During the next seven years Clover worked assiduously at his task of producing an ether inhaler. Most people know about the two ether inhalers which were described in the *British Medical Journal* in 1876 and 1877. But Clover actually produced an inhaler in 1873 which he called his " double-current inhaler." Clover described this apparatus as follows : " It consists of a facepiece without any valves : a metal box measuring 6 inches by 4, and 5 deep : and an elastic tube $\frac{5}{8}$ of an inch in diameter, to connect them. The box is either suspended by a ribbon from the administrator's neck, or placed upon the patient's bed. Inside the box is a tube of very thin copper, which conveys the expired air through it, and is then provided with a valve which opens only during expiration. The tube is broad enough to extend across the box, and undulating, in order to present a large surface, which is covered with cloth to absorb the ether. Plates of metal are so disposed as to direct the current of air, which enters through a valve during inspiration, over the surface of the tube." This description which is extracted from Clover's article in the *British Medical Journal*, (1873, i,) 283, concludes by observing: " The chief advantage of this apparatus is, however, in the comparative uniformity of mixture with air which it effects, and which, whilst securing complete quietude of the patient, prevents the unpleasant results of an over-strong dose."

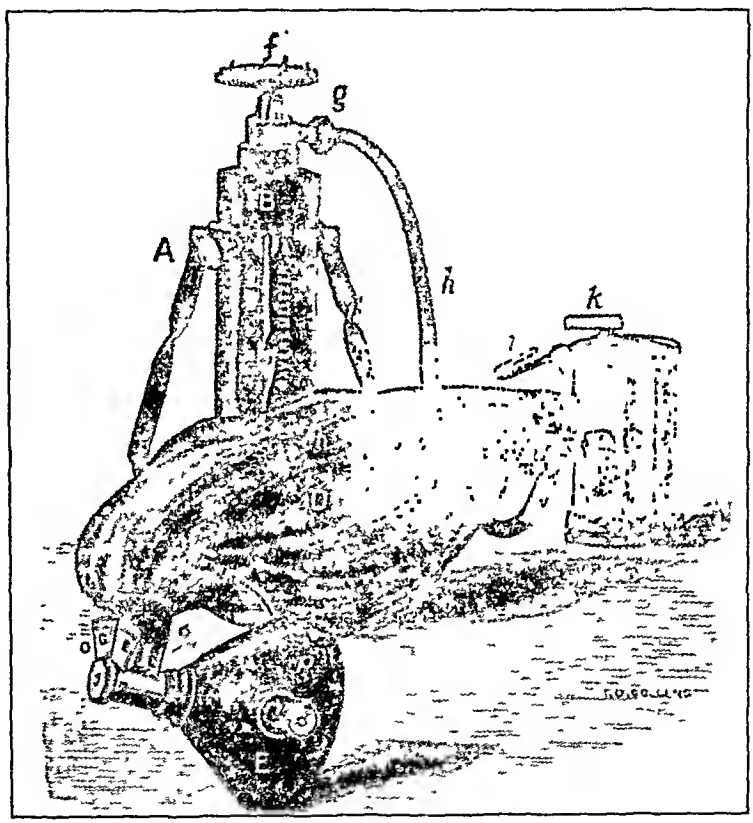
Although Clover secured good results with this apparatus, it did not achieve any great measure of popularity.

In the following year, 1874, Clover proceeded to develop an idea which he had conceived years before, and which in our humble opinion was one of his greatest contributions to the advance of anæsthetic technique and this was the securing of a comfortable and rapid induction of anæsthesia with nitrous oxide, and maintenance by the safe and efficient agency of ether.

When Clover watched the first demonstrationt of nitrous oxide in *1868* he had visualised this possibility, and in his paper read at Oxford, the M.S. of which Professor Macintosh has kindly allowed me to peruse, we find the following paragraph : " In dental operations it is often desirable to carry the inhalation to the extent of producing stertor and diminished rate of breathing, for the mouth being wide open, recovery is quicker than it could otherwise be, and although the anæsthesia may be prolonged by giving the gas by means of a nose cap, it will not always last long enough. In such cases I have sometimes commenced with the gas and then kept up the insensibility with chloroform, indeed it is a good plan to give nitrous oxide first to children and nervous patients, the insensibility thus induced does not render them unfit for chloroform, if carefully given."

In the *British Medical Journal* (1874, i, 203) Clover first described this new use of his " double-current ether inhaler."

Sir Frederic Hewitt wrote in 1893: "Clover's first plan for administering this mixture was to render the patient unconscious with nitrous oxide, and then to change the gas inhaler for an ether apparatus. His next method was to first administer nitrous oxide by itself, and then to gradually add ether by causing the gas to pass over this anæsthetic." Clover published a full description of his completed and well-known gas-and-ether apparatus in the *British Medical Journal* of July 15, 1876; it was made by Messrs. Mayer and Meltzer, and proved deservedly popular. Clover stated that he had used this apparatus with success in no fewer than 2,300 cases.




*From Duncum's Development of Inhalation Anæsthesia*

Fig. 7. Clover's "Combined Gas-and-Ether Apparatus" (1876).
A. Stand for nitrous oxide cylinder.
B. Cylinder, actuated by foot-key, *f*.
*g*. Union between cylinder and tubing, *h*.
*m*. Stopcock.

In January, 1877, Clover described his "Portable Regulating Ether Inhaler," which Frederic Hewitt describes as a "most ingenious and useful apparatus," and Dudley Buxton(5) writes: "It was mainly by the compactness and efficiency of this instrument that the practical question 'How to give ether rapidly and safely?' became answered."

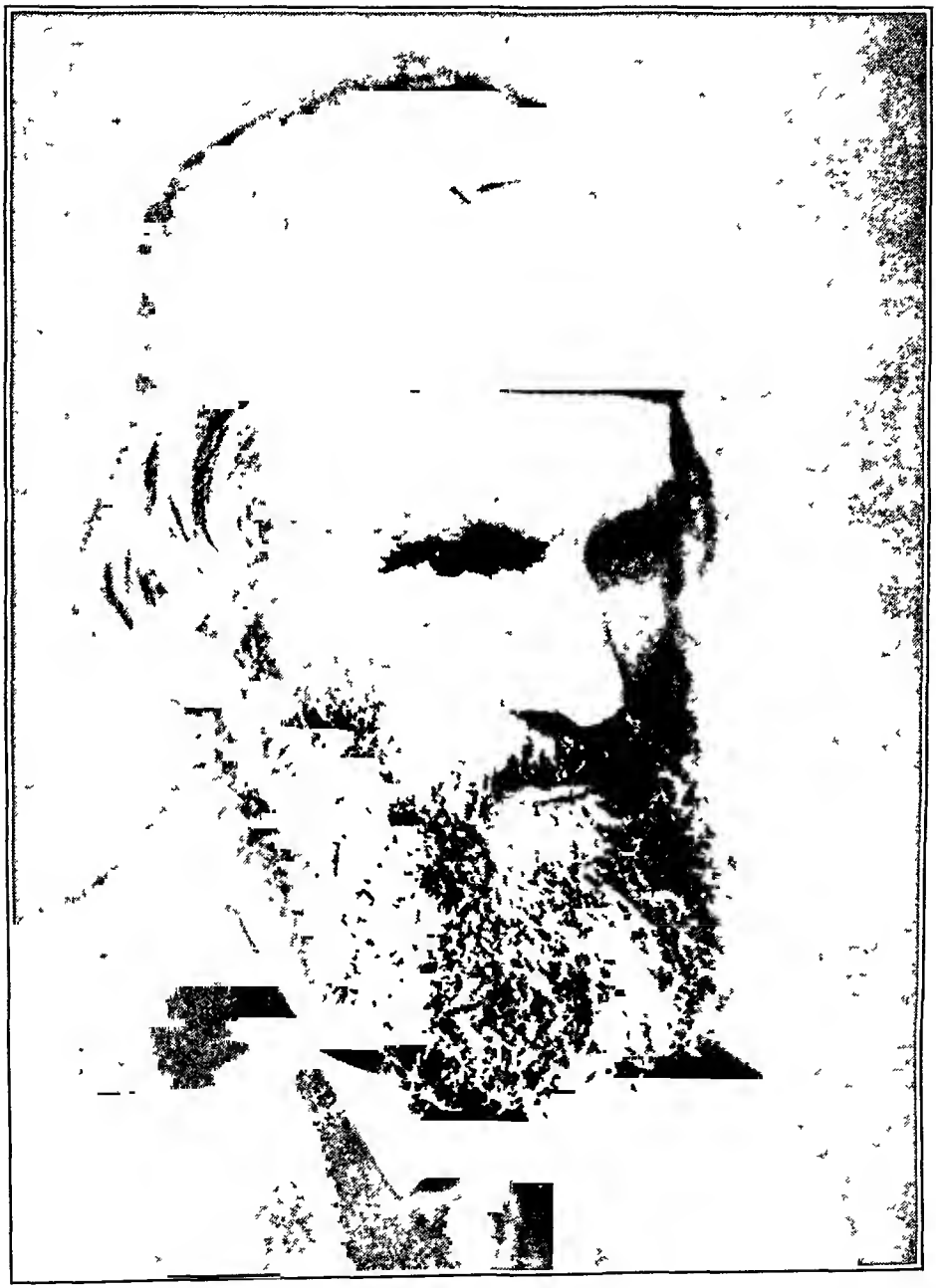


Fig 8 Joseph Clover. From a photographic portrait in the Nuffield Department of Anæsthetics, Oxford

This was his last notable contribution to the advance of anæsthesia.

In expert hands Clover's gas and ether apparatus was a great success. In my early days as a student I had the privilege of witnessing the work of the late Mr. George Rowell with this apparatus at Guy's Hospital and the smooth and comfortable passage of a patient from the conscious state to one of surgical anæsthesia was indeed a revelation. On the other hand, if the anæsthetist was not an expert, its use was accompanied by much struggling, cyanosis, excessive salivation, and sometimes vomiting. As is well known the completed Clover's apparatus of 1877 was subsequently modified and improved by many anæsthetists in many ways, and it was extensively used in this country up to the time of the first world war, when it was largely superseded by the open method, which was then succeeded by the semi-open and the closed technique with carbon dioxide absorption which prevails at the present time. But let it always be remembered that Joseph Clover was the pioneer who started this evolution of modern anæsthetic technique. Clover's contributions to anæsthesia were numerous, but I think his greatest achievement was the gradual but definite change-over from the almost universal use of chloroform in this country, with its now generally recognised dangers, to an era when ether and other safe agents are largely used for routine anæsthesia.

Clover made a contribution to surgical progress when he invented an evacuating flask and catheter for use in genito-urinary surgery, and Sir Buckston Browne paid a warm tribute to his genius in a lecture delivered before the Harveian Society of London on November 7, 1901 (R). Sir Buckston said : " No one has ever done sufficient honour to the memory of Mr. Clover. . . . In turning his attention to anæsthetics it seems to me uncertain whether that art gained or surgery lost the more. At any rate, his apparatus for evacuating stone after lithotrity is unquestionably the prototype of all modern evacuators and in it lay the germ of the whole of modern lithotrity."

After the successful introduction of his completed ether inhaler Clover had three or four very busy years, for his services as an anæsthetist were increasingly called for, and as his fame spread through this country, his attendances at committees and scientific meetings became more numerous, so much so that he had little time for rest and relaxation, and so his health, never robust, became unequal to the strain of his busy life.

Miss Clover has given me an account of the details of her father's last illness, and it seems that towards the end of 1881 his health deteriorated rapidly and in the early months of 1882 Clover was confined to his bed. On the advice of his physician, Clover was sent to a seaside resort in June, 1882, but his health did not improve and he could not leave his bed, and at his own request he returned to his home at 3, Cavendish Place on September 10 and died on September 27.

Dr. Sydney Ringer, his constant friend and medical advisor, writes : " His end was quite in keeping with his whole life—gentle, amiable,

uncomplaining, grateful to the last. The world wants one true man since he was taken away."

In an obituary in the *Lancet*(6) we read: "Every man has some few prominent points of character which give a tone to his whole life. These in Clover were his gentle modesty, his absolute unselfishness, and his active sympathy with the joys and sorrows of others."

"He had no 'push,' no ostentation or love of display. He worked steadily: his happiness consisted in honestly doing the duty which lay clear before him. None ever heard him speak harshly or unfairly of any; he was without guile or bitterness. He had lots of friends, for he made many and lost none."

In a leading article in the *British Medical Journal* of March 29, 1913, reference is made to the Hunterian Oration delivered by Sir Spencer Wells in this College on February 14, 1883, in which he said that: "Clover had during the past 20 or 30 years done more for the benefit of the world's suffering millions than almost anyone of his generation." The article concludes with these words: "Clover is unknown to the public, and it becomes all the more a duty to medicine to keep his memory green." I am sure that all the Fellows and Members of our Faculty in this College will agree with me when I beg to express the hope that the inauguration of this annual memorial lecture will in some measure keep ever green the memory of Joseph Thomas Clover.

## REFERENCES


1 SNOW, JOHN (1858), *On Chloroform and Other Anæsthetics*, page 184, John Churchill, London.

2 DUNCUM, BARBARA M. (1947), *The Development of Inhalation Anæsthesia*, chapter IX, page 253, Oxford University Press.

3 COLEMAN, ALFRED (1881), *Manual of Dental Surgery and Pathology*, chapter XIV, page 255, Smith, Elder and Co., London.

4 HEWITT, FREDERIC W. (1893), *Anæsthetics and their Administration*, part ii, chapter i, page 94, Charles Griffin and Co., London.

5 BUXTON, DUDLEY W. (1900), *Anæsthetics, Their Uses and Administration*, 3rd Ed., chapter I, page 17, H. K. Lewis, London.

6 *Lancet* (1882), 2, 597.


## THE RESTORATION AND DEVELOPMENT FUND

RECENT CONTRIBUTIONS TO the Restoration and Development Fund include a second gift from Professor C. F. M. Saint of Capetown, bringing his contribution to one hundred and ten guineas. Other gifts include one hundred guineas from J. C. Hogg of Upper Harley Street, thirty pounds from A. Michael Wood of Kenya, and twenty pounds from Admiral Sir Charles Carpendale, who for some years has been doing valuable voluntary work in the Library of the College. The total is now over £195,000.

# EARLY STAGES OF HUMAN DEVELOPMENT

Lecture delivered at the Royal College of Surgeons of England

on

31st July, 1947

by

Professor W. J. Hamilton, M.D., B.Sc., F.R.S.Ed.
Anatomy Department, Charing Cross Hospital Medical School.

## INTRODUCTION

IN 1899 PETERS DESCRIBED an early human ovum in which the villi were in the process of formation but the primitive streak had not yet appeared. The specimen was estimated by Peters to be about 3-4 days old. This estimate is obviously incorrect in the light of present-day knowledge; it is now considered to be about 13 days old. At the time of its discovery it represented the youngest known stage of human development.

In 1906 Leopold described a specimen which was younger than the Peters ovum, but no embryonic rudiment was present. Later stages of development were described by Beneke (1904) and Jung (1908); these stages confirmed the appearances in the Peters ovum but did not amplify our knowledge of early human development. Bryce and Teacher (1908) described the early development and implantation of a human ovum (T.B. 1). They estimated that the ovum was 13-14 days old (more probably 11 days). The detailed structure of this ovum is well known (see Bryce, 1924, and Teacher, 1924). It is now recognised by many embryologists as being pathological. At the time (1908) when first described it was considered to make a definite contribution to our knowledge of human embryology. In 1913 Miller gave a brief description of an early human embryo found in fragments of the endometrium after curettage for the relief of dysmenorrhœa. Unfortunately, only five sections were preserved. A fuller description of this ovum was given by Streeter in 1926. The histological preservation was good and the embryo was estimated to be about 11 days old. For details of other ova previous to this date, reference should be made to the monographs of Bryce (1924) and Streeter (1926).

In 1930 Allen *et al.* succeeded in obtaining five unsegmented ova by reverse irrigation of the uterine tube from the uterus. Since that date a number of investigators have obtained unsegmented living tubal ova. For details and literature the reader is referred to the publications of Hamilton (1944) and Rock and Menkin (1944) and Rock and Hertig (1948).

A well-preserved embryo, aged about 11 days, was described by Stieve (1936) and an almost complete embryo was described by Dible and

West in 1941. However, the outstanding contribution to our knowledge of human development from 7½-16 days has been made by the researches of Hertig and Rock (1941, 1944 and 1945) and Rock and Hertig (1942, 1944 and 1948). Other early human embryos have recently been described by Hamilton *et al.* (1945), Davies (1944), Marchetti (1945) and Heuser *et al.* (1945).

## UNSEGMENTED EGGS

Soon after ovulation the ovum with its surrounding còrona radiata passes into the uterine (Fallopian) tube. (Fig. 1.)

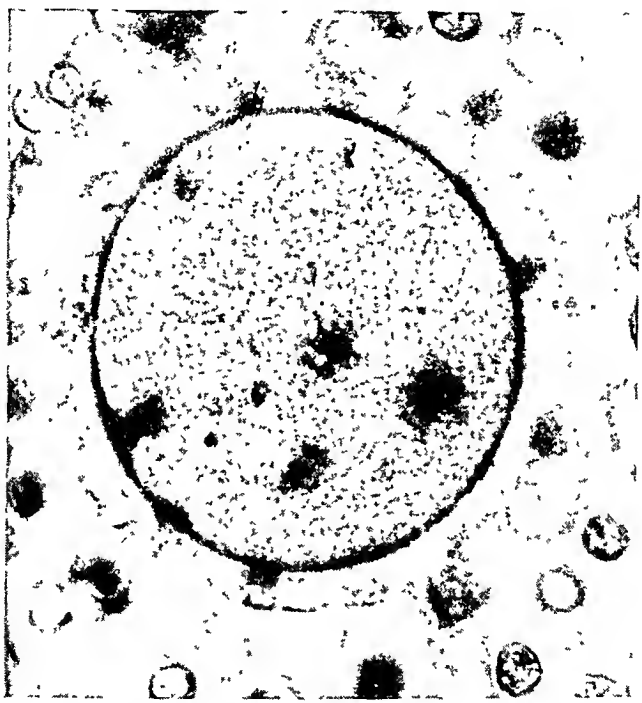


Fig. 1. Photomicrograph of a living human ovum, surrounded by the corona radiata, recovered from the uterine tube. X.C.

A number of unsegmented ova at this stage have been described (see Hamilton, 1944, Rock and Hertig, 1944, for literature). The corona cells are loosely applied to the zona pellucida. In the living egg the zona has a homogeneous appearance and is closely applied to the vitellus. After fixation and staining, the zona undergoes a contraction and appears bluish-pink when stained with hæmatoxylin and eosin. The vitellus in the recently ovulated living egg is yellowish in colour, uniformly granular, and does not have a polar distribution as occurs in some other mammalian eggs. In ova which are undergoing degenerative changes coarse and fine granular zones become evident in the vitellus (see Rock and Hertig,

1944). In the living human ovum the nucleus is not visible by transmitted light. By the time of ovulation the nucleus is at the stage of the second maturation division and can be seen in sectioned material. (Fig. 2.) It cannot be stated at present whether the second maturation division is completed in the absence of fertilization, but it is probable that this division is not complete in the absence of fertilization and in this respect the human ovum agrees with what is known to occur in most mammalian eggs.

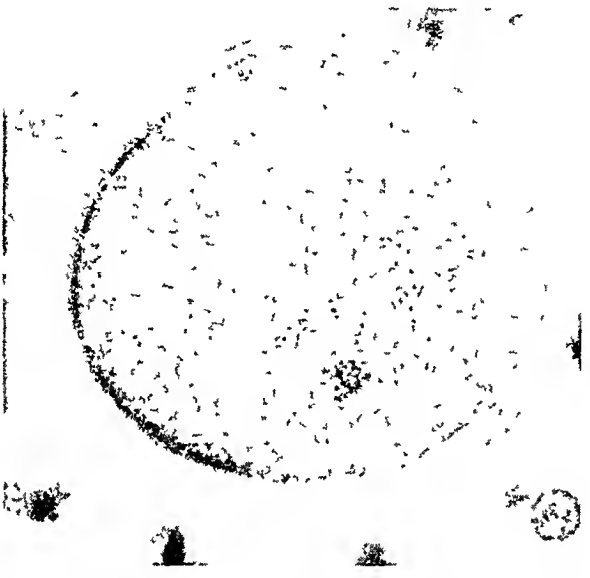


Fig. 2. A section of the ovum shown in Fig. 1. It shows the second maturation division X.C.

## FERTILIZED OVA

An ovum at an early stage of fertilization was described by me in 1944. It shows sperms passing through the zona pellucida (Fig. 3.) A second ovum with pronuclei was recovered on April 3, 1944. It was found on the 17th day of the menstrual cycle. (Fig. 4.) In vitro fertilized 2-3 cell stages were described by Rock and Menkin (1944). When these ova were examined after incubation two blastomeres of " fairly uniform size and appearance " were found in two specimens and three blastomeres in a third. From the examination of one of the sectioned ova it is evident that the cells are undergoing degenerative changes. An abnormal segmenting ovum was discovered by me on January 11, 1944, after flushing the uterine tube on the 18th day of the menstrual cycle. It consists of a group of small cells (?) in one half of the zonal cavity and a large cell in the other half. (Fig. 5.) When sectioned and stained it

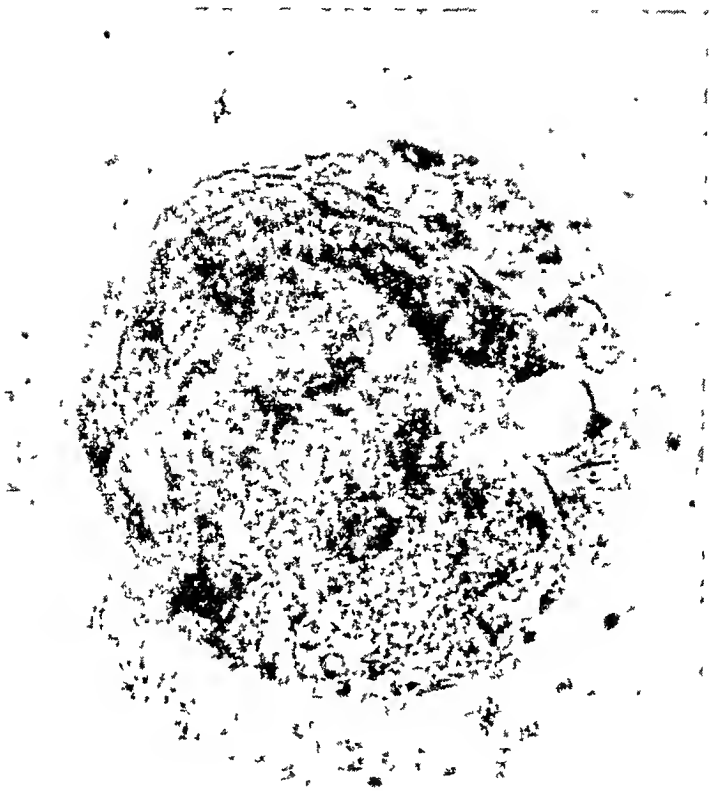


Fig. 3. Photomicrograph of a living human ovum recovered from the uterine tube. Sperms are seen in the zona pellucida. X.C.

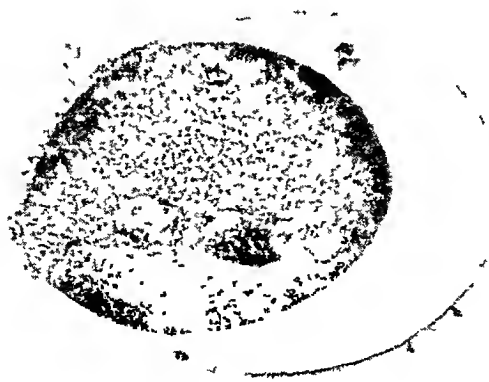


Fig 4. A section of an ovum showing pronuclei. X C

Fig. 5. Photomicrograph of a living human ovum showing one blastomere and a number of small cells. X.C.

was evident that the small cells (?) had undoubtedly been derived from one of the first blastomeres by fragmentation. The other blastomere was also undergoing degenerative changes. Rock and Hertig (1948) have recovered three segmenting ova, one consisting of eight blastomeres and assumed to be about 72 hours old; another consisting of nine blastomeres is probably 84 hours old and may be abnormal; the third has 12 blastomeres and is probably normal, but no details have yet been published about this egg. It is deduced from this material that the duration of cleavage in the human ovum occupies 72 hours. Stages between that of the 12-blastomere stage and the 7½-day partially implanted embryo described by Hertig and Rock (1945) are unknown.

## IMPLANTING OVA

It is estimated that the human blastocyst becomes attached to the endometrium on the sixth day after ovulation. The youngest stage of implantation yet described (Rock and Hertig, 1942, 1945) is superficially implanted and is only partially covered by maternal endometrium. The blastocyst consists of the trophoblast and embryonic (inner cell) mass.

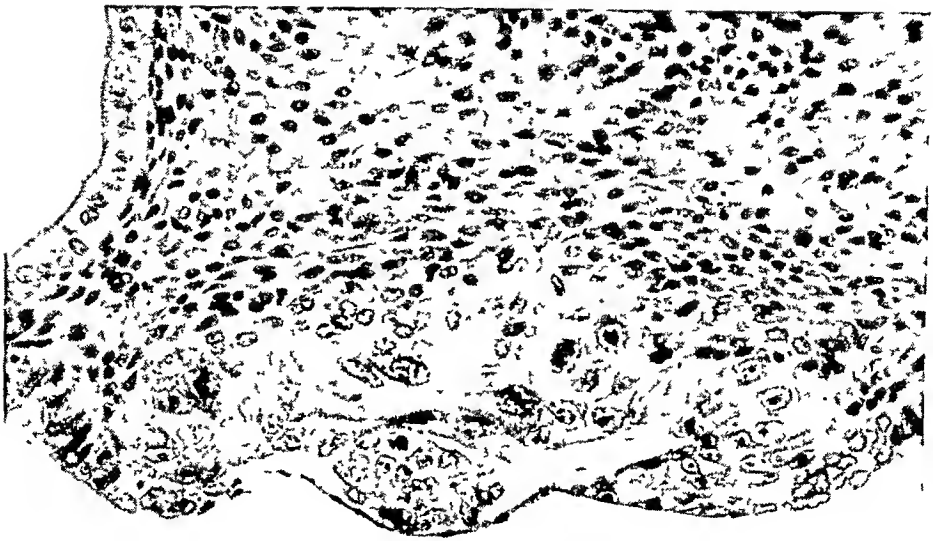


Fig. 6. A section through the middle of the Hertig-Rock embryo (No. Mu 8020) estimated to be 7½ days old. The trophoblast consists of a thick proliferating disc growing into the endometrial stroma and a thin mesothelial-like layer. The inner cell mass is represented by an oval mass of cells. X.C. (Reproduced by courtesy of Drs. Hertig and Rock.)

(Fig. 6.) The trophoblast varies from a thick proliferating disc of syncytioblast and cytotrophoblast adjacent to the embryonic mass and a thin mesothelial-like layer at the abembryonic pole. This latter layer has not yet penetrated into the endometrium and so depicts the structure of the wall of the blastocyst before implantation. The mesothelial-like layer is collapsed and applied to the surface of the embryonic mass. Trophoblastic cells at the edges of the proliferating disc and in contact with the maternal tissue are hypertrophied but with the cell boundaries distinct. The cells over the embryonic mass are differentiating into " primitive " cytotrophoblast and syncytiotrophoblast, but lucunæ formation has not yet begun. The embryonic mass consists of a layer of polyhedral ectodermal cells and a layer of vesicular endodermal cells. Between the ectodermal cells and the trophoblast there are two clefts which represent the primordium of the amniotic cavity. Amniogenic cells are being delaminated from the cytotrophoblast in the region of the embryonic mass.

The next known stage of human development is shown by the Hertig and Rock embryo (No. Wi 8004) which is estimated to be about 9½ days after ovulation. The blastocyst is more than two-thirds implanted into the endometrium. The entire trophoblastic wall has undergone proliferative changes; these, however, are more prominent on the embryonic than abembryonic wall. (Fig. 7.)

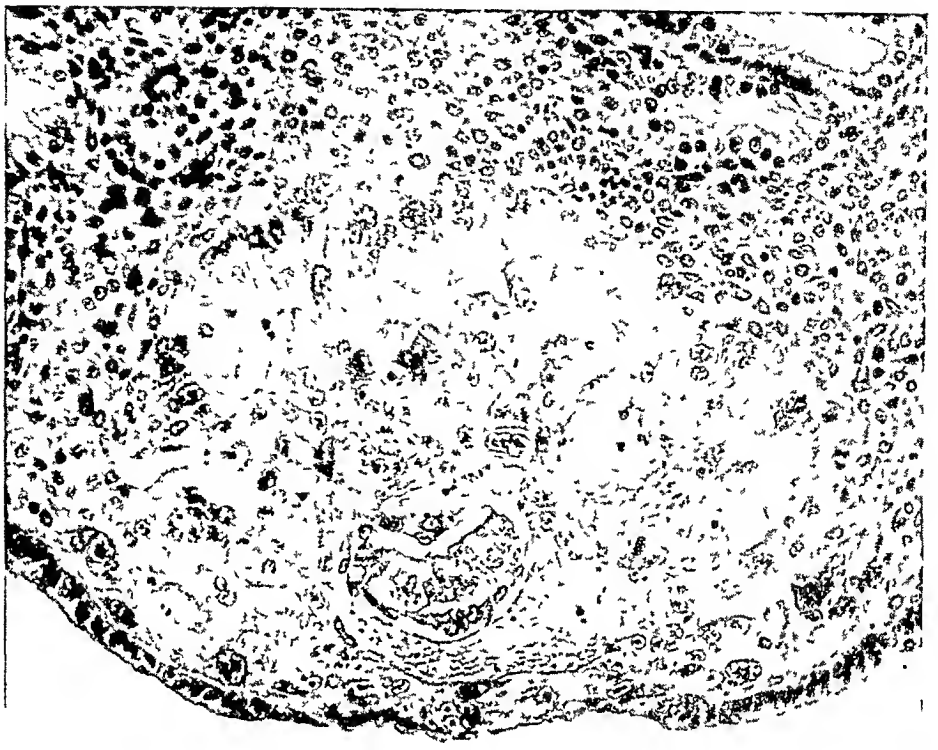


Fig 7. A section through the middle of the Hertig-Rock embryo (No. Wi 8004) estimated to be 9½ days old. Lacunæ have developed in the trophoblast (Reproduced by courtesy of Drs. Hertig and Rock)

Numerous and irregular slit-like lacunæ are developing in the deeper parts of the syncytiotrophoblast. Many of the lacunæ contain maternal blood and intercommunicate and thus constitute the beginning of an intervillous circulation. The junction between the syncytiotrophoblast and the maternal tissue has an irregular contour, due to the invasion of the latter by pseudo-podial outgrowths from the former. The embryonic mass is composed of a bilaminar disc of columnar ectodermal cells and a cap of endodermal cells. The amniotic cavity is beginning to form. Mesodermal cells are differentiating from the inner aspect of the cytotrophoblast.

During the next three days (10, 11 and 12) the ovum becomes almost completely surrounded by the maternal endometrium. The defect in the uterine epithelium, caused by its penetration by the ovum, is gradually closed by a coagulum of fibrin and by the proliferation of the adjacent endometrial epithelium over the fibrin. A number of well-preserved ova have been described which show this stage of development (see Hertig and Rock, 1941 and 1945) and Hamilton *et al.* (1945) for literature. The

syncytiotrophoblast, especially in the deeper parts, continues to proliferate rapidly and forms approximately three-fourths of the trophoblastic covering of the ovum. The peripheral part of the syncytiotrophoblast invades and absorbs the œdematous endometrial tissue and extravasated blood to make room for the enlarging ovum. The blood and maternal tissue so absorbed is a source of nutrition for the embryo and the membranes. Maternal capillaries are invaded by the advancing trophoblast so that maternal blood can readily flow into the enlarging lucunæ. The cytotrophoblast forms about one-quarter of the trophoblastic wall and for the greater part of its extent is made up of a single layer of cuboidal cells.

The embryo at this stage is composed of a bilaminar disc of opposing ectoderm and endoderm and is aproximately circular in outline. The longitudinal axis of the embryo is not yet apparent. The ectoderm is composed of columnar cells which are vertically arranged in respect to the horizontal axis of the embryo. At the edge of the embryonic disc they are continuous with the flattened amniotic cells. (Figs. 8 and 9.)

Fig. 8. A photogramograph of an 11½-day human embryo embedded in the endometrium. The inner cell mass has differentiated into the embryonic ectoderm and endoderm. Heuser's membrane and the embryonic endoderm enclose the primary yolk sac. X.C. (Reproduced by courtesy of Drs. Hertig and Rock.)

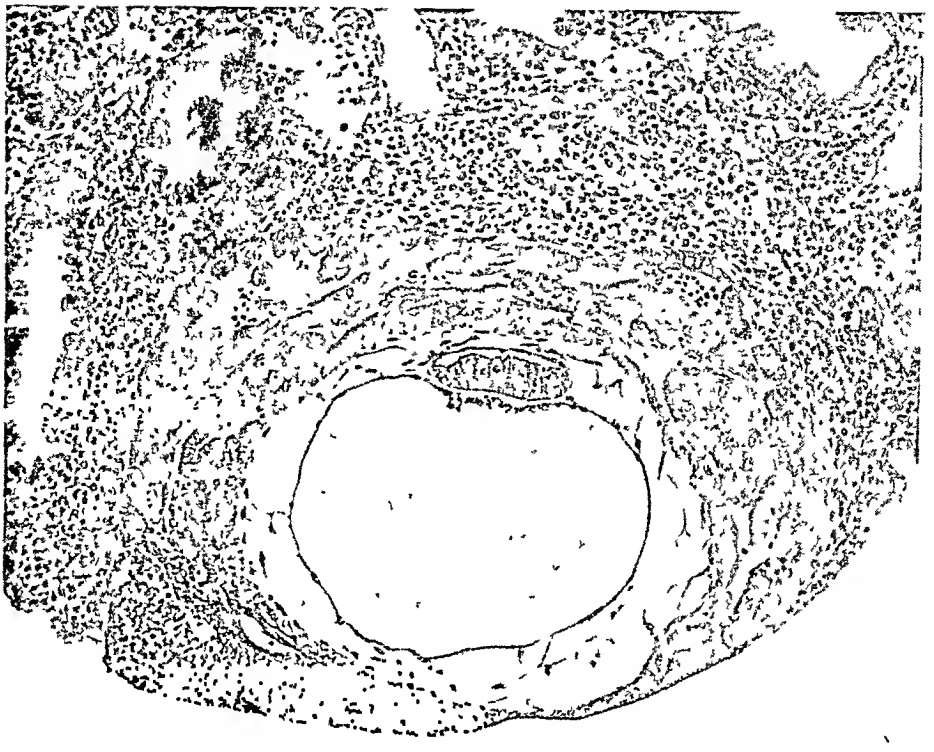


Fig. 9. A photomicrograph of a 12-day human embryo embedded in the endometrium. (Reproduced by courtesy of Drs. Hertig and Rock)

Amniogenic cells are in the process of differentiating from the cytotrophoblast. The endodermal cells are of approximately the same extent as the ectodermal cells. Their relations vary considerably in the different embryos described. In the Hertig and Rock embryo No. 7699 they form a mass of from one to three layers thick (Fig. 8), but in the Hertig and Rock embryo No. 7700 they form a single layer. (Fig. 8.) In the Barnes embryo (Hamilton *et al.*, 1943) they are heaped up to form a layer several cells thick at one side of the embryonic disc. (Fig. 10.)

In addition to the embryonic mass the chorionic cavity is filled to a varying extent with primitive mesoblast, magma reticulare. This tissue is composed of stellate cells in the form of a network. The innermost layer of the mesoblast becomes condensed to form a mesothelial membrane or Heuser's membrane. At the edge of the embryonic disc this membrane is continuous with the endoderm. The space enclosed by the endoderm and mesothelial membrane is the primary yolk sac. (Fig. 11.) It will be seen that these cells lining the primary yolk sac have two distinct origins, cuboidal endodermal cells derived from the embryonic mass and mesothelial cells derived from the mesoblast. Within this primary yolk sac is a granular eosinophilic precipitate.

Fig. 10. A general low-power view of the Barnes embryo estimated to be about 10½ days old. The extent of the syncytio-and cytotrophoblast in the different parts of the vesicle is shown. The embryonic rudiment has differentiated into columnar ectoderm and embryonic endoderm, the latter is continuous with Heuser's membrane. The extra-embryonic mesoblast has been artificially separated from the cytotrophoblast. X.C.

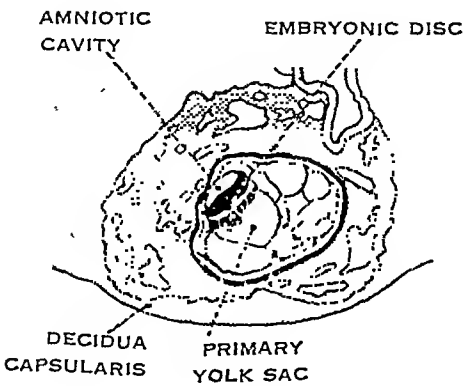



Fig. 11. Diagram to show the development of the amniotic cavity and primary yolk sac.

There has been much speculation and conjecture concerning the origin of the primitive mesoblast. Hill (1932) and Florian (1933) were of the opinion that this mesoblast is precociously developed allantoic mesoblast, as in *Tarsius*, and that it arises from amniotic ectoderm posterior to the site of the future cloacal membrane. In the human subject it develops before the appearance of the primitive streak. The extensive investigations of Hertig (1935) Wislocki and Streeter (1938), Heuser and Streeter (1941), Hertig and Rock (1941 and 1945), seem to point to its origin from the inner aspect of the cytotrophoblast. At the abembryonic pole where the trophoblast is least differentiated the cytotrophoblastic cells are unevenly arranged and appear to be intimately connected with the delaminating mesoblast. In many places the processes of the peripherally placed stellate mesoblastic cells are continuous with the cytotrophoblast.

During the next few days a number of important changes occur in the chorion and embryo. The syncytiotrophoblast lining the lacunar spaces and covering the cytotrophoblast now forms the greater part of the chorion. Syncytial streamers from the trophoblast pass into the endometrium. Outgrowths of the cytotrophoblast occur and form the primary villi. These villi later form the cytotrophoblastic columns. Soon a core of mesoblast appears in each primary villus to convert it into a secondary villus. The chorionic mesoblast which is increasing in amount is soon separated into somatopleure and splanchnopleuric layers by the appearance of the extra-embryonic cœlom. (Fig. 12.) The splanchnopleuric layer forms the outer layer of this secondary yolk sac. In the Marchetti embryo, estimated to be about 13 days old, the extra-embryonic cœlom has not yet appeared, while it is well formed in the Carnegie embryo No. 7801 (Heuser *et al.*) estimated to be about 13½ days old.

As a result of axial differentiation the embryonic disc becomes oval in outline, the long axis being in the antero-posterior axis of the embryo. The axial differentiation is due to the appearance of the primitive streak at the candal part of the disc. (Fig. 13.) Cells from the primitive streak proliferate as a downgrowth between the ectoderm and endoderm. At the anterior end of the primitive streak Hensen's node soon differentiates and gives origin to the head process. The amniotic cavity increases in size and is now composed of a layer of flattened cells covered by a coat of mesoblast. The primary yolk sac of the earliest stage becomes transformed into a secondary yolk sac as the result of the appearance of an inner layer. The secondary yolk sac is relatively smaller than the primary yolk sac. The cells of this inner layer resemble those of the embryonic endoderm and are continuous with it; whether these cells are derived from the embryonic endoderm by migration or by differentiation from the mesothelial cells of Heuser's membrane is still in doubt. The distal part of the primary yolk sac may become detached from the proximal part with the expansion of the extra-embryonic cœlom and in many embryos forms an isolated vesicle in the extra-embryonic cœlom. (See Bryce, 1924, and Heuser *et al.*, 1945, for literature.)

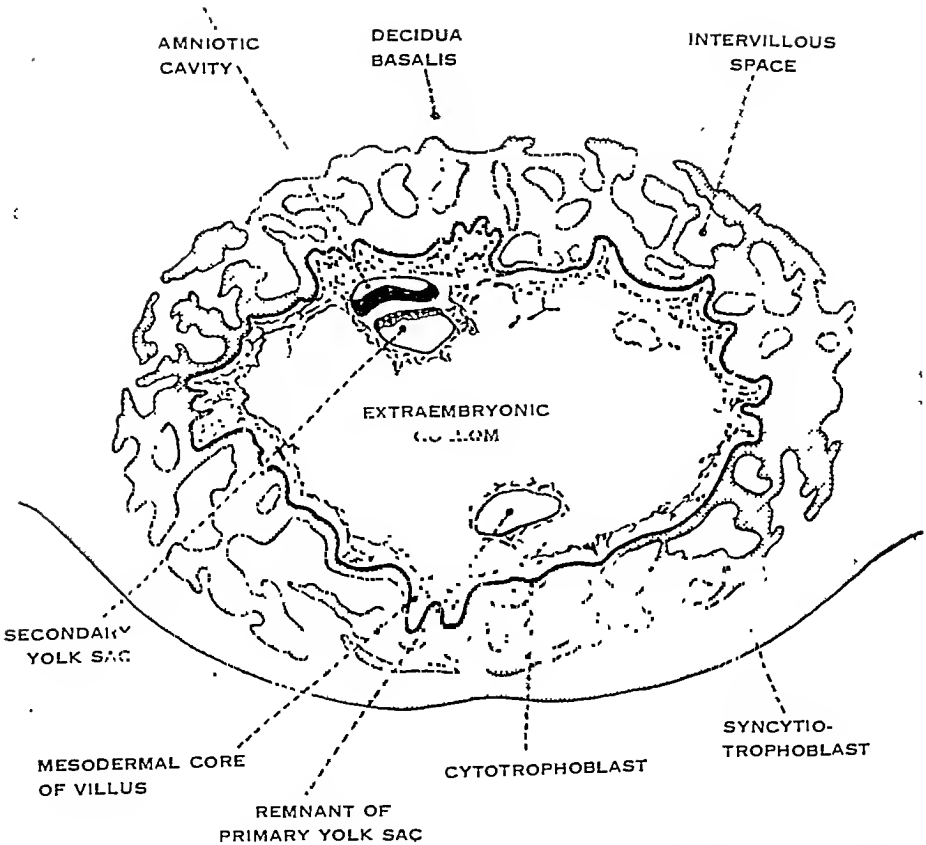



Fig. 12. Diagram to show the development of the secondary yolk sac, extra-embryonic cœlom and remnant of the primary yolk sac.

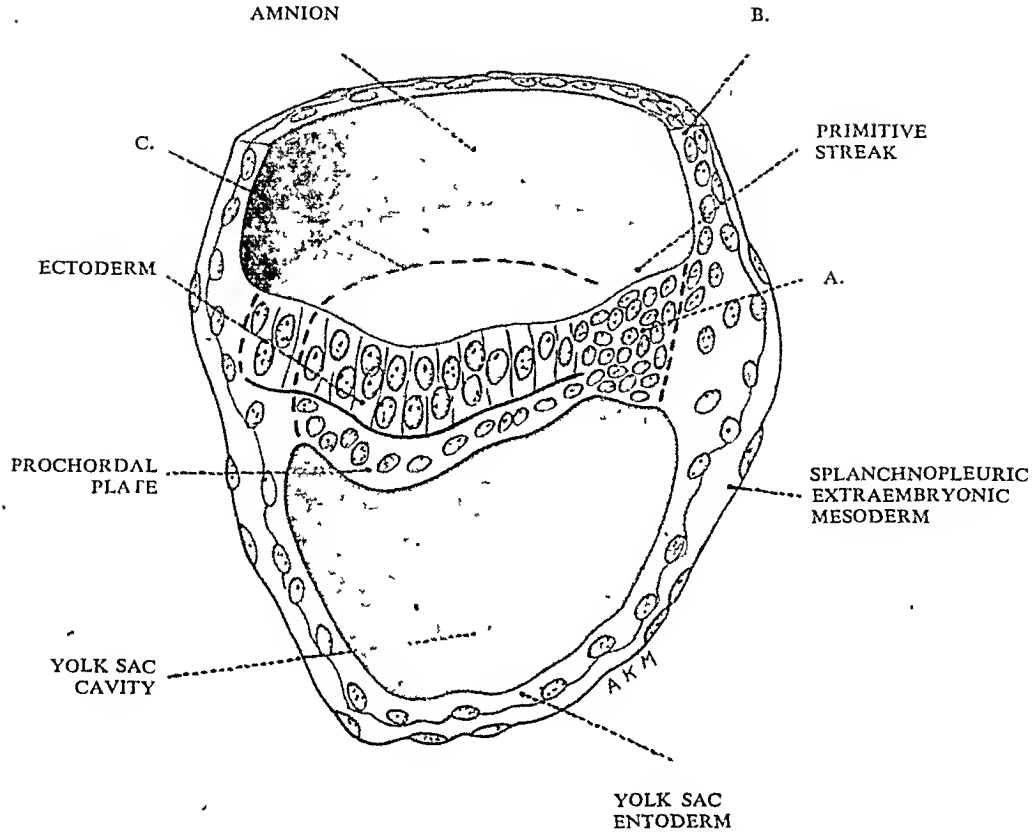



Fig. 13. A sectioned schematic dimensional reconstruction of an embryo at the time of the appearance of the primitive streak.

## REFERENCES

ALLEN, E., PRATT, J.P., NEWELL, Q. U., and BLAND, L. J. (1930) Human tubal ova; related early corpora lutea and uterine tubes. *Contr. Embryol., Carneg. Instn., Wash.*, **22**, 45.

BENEKE, R. (1904) Ein sehr junges menschliches Ei. *Monatsschr. f. Geburtsh. u. Gynak.*, **22**, 771.

BRYCE, T. H. (1924) Observations on the early development of the human embryo. *Trans. Roy. Soc., Edin.*, **53**, 533.

——— and TEACHER, J. H. (1908) *Contributions to the study of the early development and imbedding of the human ovum.* Maclehose, Glasgow.

DAVIES, F. (1944) A pre-villous human ovum, aged nine to ten days (the Davies-Harding Ovum). *Trans. Roy. Soc., Edin.*, **61**, 315.

DIBLE, J. H., and WEST, C. M. (1941) A human ovum at the pre-villous stage. *J. Anat., Lond.*, **75**, 269

FLORIAN, J. (1933) The early development of man, with special reference to the development of the mesoderm and cloacal membrane. *J. Anat., Lond.*, **67**, 263.

HAMILTON, W. J. (1944) Phases of maturation and fertilization in human ova. *J. Anat., Lond.*, **78**, 1.

——— BARNES, J., and DODDS, H. (1943) Phases of maturation, fertilization and development in man. *J. Obstet. Gynec., Brit. Emp.*, **50**, 241.

——————— Boyd, J. D., and Mossman, H. W. (1945) *Human Embryology*. Heffer, Cambridge.

Hertig, A. T. (1935) Angiogenesis in the early human chorion and in the primary placenta of the macaque monkey. *Contr. Embryol., Carneg. Instn., Wash.*, 25, 37.

——————— and Rock, J. (1941) Two human ova of the pre-villous stage having an ovulation age of about 11 and 12 days respectively. *Contr. Embryol., Carneg. Instn., Wash.*, 29, 127.

——————— (1944) On the development of the early human ovum, with special reference to the trophoblast of the pre-villous stage : a description of seven normal and five pathologic human ova. *Amer. J. Obstet. Gynec.*, 47, 149.

——————— (1945) Two human ova of the pre-villous stage having a developmental age of about seven and nine days respectively. *Contr. Embryol., Carneg. Instn., Wash.*, 31, 65.

Heuser, C. H., Rock, J., and Hertig, A. T. (1945) Two human embryos showing early stages of the definitive yolk sac. *Contr. Embryol., Carneg. Instn., Wash.*, 31, 85.

——————— and Streeter, G. D. (1941) Development of the macaque embryo. *Contr. Embryol., Carneg. Instn., Wash.*, 29, 15.

Hill, J. P. (1932) The developmental history of the Primates. *Phil. Trans. Roy. Soc., Lond.* B, 221, 45.

Jung, P. (1908) Beitrage zur frühesten Ei-Einbettung beim menschlichen Weibe. *Karger, Berlin.*

Leopold, G. (1906) Ueber ein sehr junges menschliches Ei in situ. *Hirzel, Leipzig.*

Marchetti, A. A. (1945) A pre-villous human ovum accidentally recovered from a curettage specimen. *Contr. Embryol., Carneg. Instn., Wash.*, 31, 107.

Miller, J. W. (1913) Corpus luteum und Schwangerschaft. Das jüngste operativ erhaltene menschliche Ei. *Berl. klin. Wschr.* 50, 865.

Peters, H. (1899) *Ueber die Einbettung des menschlichen Eies.* Deutike, Leipzig und Wien.

Rock, J., and Hertig, A. T. (1942) Some aspects of early human development. *Amer. J. Obstet. Gynec.*, 44, 973.

——————— (1944) Information regarding the time of human ovulation derived from a study of three unfertilized and 11 fertilized ova. *Amer. J. Obstet. Gynec.*, 47, 343.

——————— (1948) The human conceptus during the first two weeks of gestation. *Amer. J. Obstet. Gynec.*, 55, 6.

——— and Menkin, M. F. (1944) In vitro fertilization and cleavage of human ovarian eggs. *Science*, 100, 105.

Stieve, H. (1931) Ein ganz junges, in der Gebarmütter erhaltenes menschliches Ei (Keimling Werner). *Z. mikr.-anat. Forsch.*, 40, 281.

Streeter, G. L. (1926) The Miller Ovum. The youngest normal human embryo thus far known. *Contr. Embryol. Carneg. Instn., Wash.*, 18, 33.

Teacher, J. H. (1924) On the implantation of the human ovum and the early development of the trophoblast. *J. Obstet. and Gynec., Brit. Emp.*, 31, 166.

Wislocki, G. B., and Streeter, G. L. (1938) On the placentation of the macaque (Macaca mulatta), from the time of implantation until the formation of the definitive placenta. *Contr. Embryol., Carneg. Instn., Wash.*, 27, 1.

# CONGENITAL OBSTRUCTION AT THE BLADDER NECK

Hunterian Lecture delivered at the Royal College of Surgeons of England

on

2nd February, 1948

by

A. W. Badenoch, M.A., M.D., Ch.M., F.R.C.S.
Surgeon to St. Peter's Hospital
Assistant Surgeon to St. Bartholomew's Hospital

THERE ARE CERTAIN conditions fairly commonly found in infancy and early childhood which may lead to obstruction of the outflow of urine, such as a severe degree of phimosis or meatal stenosis. These conditions are easily recognised and equally easily dealt with.

There are less common forms of obstruction:

1. Stenosis of the internal meatus of the bladder.
2. Valves in the posterior urethra, about the level of the verumontanum.
3. Enlargement of the verumontanum.
4. Congenital stricture of the anterior urethra.
5. Diverticulum of a seminal vesical.

The more severe the obstruction, the earlier it will manifest itself, and many if not most infants and young children in whom these conditions are diagnosed, are in an advanced stage of uræmia and die before or in adolescence.

Diverticulum of the seminal vesical is very rare and of considerable embryological interest, since it may represent an undeveloped ureteric bud.

Congenital stricture of the urethra is also rare. It can, of course, occur in any part of the canal, but is more often found in the region of the bulb. Apparently, when it has been completely divided there is no tendency for it to reform, and it is probably the only type of urethral stricture which can be cured by simple division or dilation, on one occasion.

Hypertrophy of the verumontanum was first reported by Bugbee and Wolfstein in 1923. Meredith Campbell (1937) records 15 instances discovered at autopsy, and other series have been reported. It appears to be a condition almost limited to infancy or to early childhood.

Urethral valves were first described as a cause of obstruction by Langenbeck in 1802, but it was not until 1912 when Young published a considerable series, that it became generally realised that it was not excessively rare.

Three types are described: (1) the supra-montanal, and (2) infra-montanal—in each of which the valve may occlude the whole or only half of the urethra; and (3) the iris form, which corresponds to a stricture elsewhere in the urethra. Nearly all the recorded cases have occurred in childhood, and it is undoubtedly a lethal form of obstruction.

The main substance of this paper is concerned with stenosis at the bladder neck which is the only common form of congenital obstruction of the lower urinary tract met with in adults. That obstruction can occur in this situation from causes other than enlargement of the prostate has been known for many years. In 1833, G. J. Guthrie (President of the Royal College of Surgeons on three occasions) described the condition in a lecture at the Westminster Hospital. Guthrie has other claims to fame as he was the first British surgeon to use a lithotrite. His interests were by no means confined to urology, since he founded a hospital for Diseases of the Eye, which is now the Royal Westminster Ophthalmic Hospital. In this and other lectures, and in his book on Diseases of the Bladder Neck, Guthrie described this form of obstruction extremely well. He stated that the under part of the vesical orifice presents a bar, or dam, which produces marked obstruction and leads to the formation of pouches; that it may commence at an early period of life, although it is more commonly met with in later years. He does not ascribe the condition to a congenital origin, but believed it was due to inflammation at the neck of the bladder producing contraction and loss of elasticity.

A few years later, Mercier also described the condition as occurring in young men and as having the same effect on the urinary outflow as the prostatic enlargement of older men. Subsequently most French writers considered that the clinical condition was due to lack of bladder tone and atrophy of the bladder musculature, rather than to obstruction and they gave the condition the name "prostatisme sans prostate." In America, Keyes, Fuller and Chetwood recognised the obstructive condition of the bladder neck and considered it was due to contracture or stricture at the prostatic urethra. In 1913, Young reported 52 cases of bladder neck obstruction of whom 17 were under 50 years of age. It has been called a median bar obstruction, a fibrous bar or a fibrous prostate.

In 1927, Marion reported four cases of bladder neck obstruction all of whom had had symptoms since adolescence. He considered the condition was a hypertrophy of the internal sphincter at the bladder neck, and was the first to attribute it to a congenital factor. At St. Peter's Hospital and elsewhere, the condition has since been known as Marion's Disease.

I have a personal series of 26 cases of bladder neck obstruction which I believe to be congenital in origin. These cases are all males, although the condition can occur in women. The average age was 43; 16 were under 50, the youngest being seven; only two were over 60 years of age.

In no case was there any enlargement of the prostate to feel on rectal examination or to see on cystoscopy. About half the patients had been previously examined and investigated elsewhere without deriving benefit. In nearly every case after operation the patient has remarked that "never in his life had he passed water like this." All the cases except one were associated either with diverticulum of the bladder or bilateral hydro-ureter.

There is often a history going back for many years, and sometimes for as long as the patient can remember, of difficulty in passing water. This difficulty may be in starting, it may be that the stream is poor, or it may be that there is a feeling that he has failed to empty the bladder. In some cases there is an acute exacerbation of symptoms owing to the occurrence of infection in the bladder. There is then marked frequency with a burning pain in the urethra during and at the end of the act, and spasm in the bladder region and perineum of very great severity, with marked difficulty in starting. Once infection has occurred in the bladder it cannot be cleared up completely by medicinal means alone.

Eleven cases presented with retention, in three the onset was acute, and in eight it was chronic with over-flow and nocturnal eneuresis. Nine cases presented with recurrent attacks of cystitis. Three had a suprapubic fistula following operation elsewhere, and three presented with hæmaturia, one being complicated by a growth and two by stones. If there is chronic or acute retention and infection supervenes, this may become very severe indeed, with a high temperature, rigors and evidence of severe toxæmia, necessitating open drainage as an urgent measure. This occurred in two patients who were admitted with sterile urine, they were catheterized with the usual precautions, yet within two days of admission there was a swinging temperature up to 103°F.-104°F., and frank pus could be seen in the urine. In no case in this series—either in the acute or chronic retention—was the blood urea raised over 50 mgms. and rarely was it over 40 mgms. per 100 m.l.

The diagnosis is suggested by the age of the patient, by the long history, by the absence of any obvious obstructive factor, and by the presence of a diverticulum or of bilateral hydro-ureter. I have only seen two diverticula of the bladder which were not associated with obstruction of the lower urinary tract. One was at the fundus, a urachal or true congenital diverticulum, and the other was from traction by adhesions following repair of an inguinal hernia. In both these cases the neck was fairly wide. In this series, 23 cases were accompanied by one or more diverticular of the bladder—46 diverticula in all. Of the other three, two had bilateral hydro-ureter with a marked degree of residual urine, and the other had chronic retention with nocturnal eneuresis. (Fig. 1.)

I have not seen a diverticulum in the presence of a large adenomatous prostate, and I have made enquiries of my senior colleagues at St. Peter's Hospital, who tell me that in their experience it is exceptional to get a true diverticulum with a large adenomatous prostate. There may often be a tremendous enlargement of the gland without much in the way of obstruction. (Fig. 2.)

The diagnosis is confirmed by cystoscopy. When the condition is present a collar can always be demonstrated at the internal meatus with an ordinary Ringleb examining cystoscope, the eyepiece being depressed as the tip of the cystoscope reaches the meatus. It may, of course, be

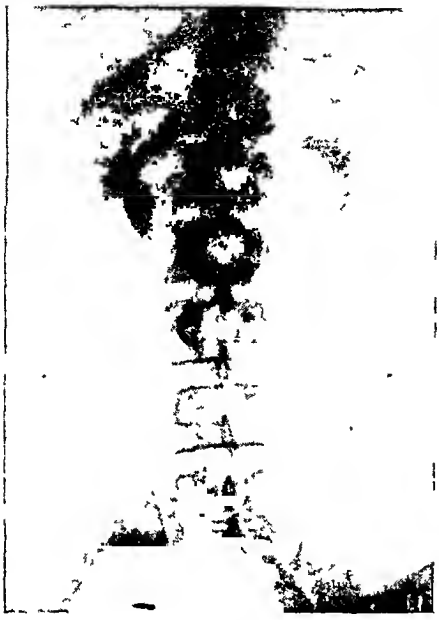


Fig. 1. Bilateral hydronephrosis and hydro-ureter, and bladder - neck obstruction.

Fig. 2. A large filling defect from enlargement of the prostate, without any obstruction of the upper urinary tract.

possible to demonstrate a collar which is not causing obstruction, but in this case if the patient is asked to pass water, the trigone is seen to depress, the posterior arc of the internal meatus opens and the bar disapears. In congenital hypertrophy at the bladder neck this does not occur, and the collar remains closed when the patient attempts to micturate.

The cystoscopic appearance is quite different in enlargement of the prostate. When the median lobe is mainly affected there is a rounded intra-vesical projection, and with enlarged lateral lobes there is a well-marked cleft or " V " anteriorly at 12 o'clock, differing from the rounded appearance of the normal internal meatus.

In the neurogenic bladder the meatus is entirely different, being wide open and funnel-shaped, and both ureteric orifices may even be seen in the same field as the verumontanum with an ordinary examining cystoscope.

With a slight degree of obstruction only a little trabeculation is seen on cystoscopy, but in the more advanced stages this becomes very marked with thickened raised ridges, and numerous sacculations which often contain pus and phosphatic debris. (Figs. 3 and 4.) In the most severe degree of obstruction the inter-ureteric bar stands out prominently in the bladder and there is a well-marked depression between this and the neck. Trabeculation in a neurogenic bladder is as a rule, much finer in texture.

Fig. 3
Moderate degree of trabeculation of the bladder wall with diverticulum. The gap between the diverticulum and the bladder shows the thickness of the neck.

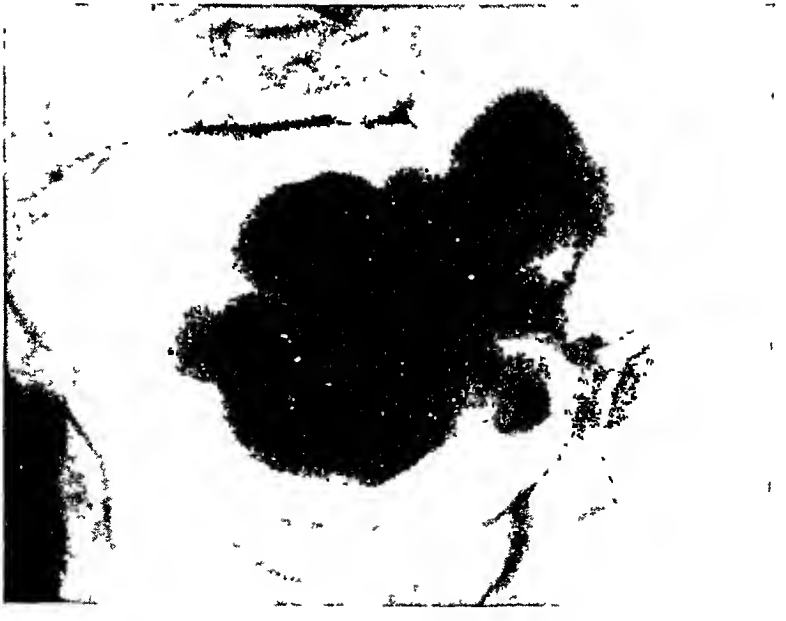


Fig. 4
An advanced degree of obstruction showing marked sacculation of the bladder.

The orifice of a diverticulum can be easily identified and its appearance is quite typical. It is never possible to see the bottom from inside the bladder, whereas the floor of a sacculation can always be seen on proper manipulation of the cystoscope. Diverticula may be single or multiple and nearly all those associated with obstruction open in the region of a ureteric orifice. The latter may be on the edge of the diverticulum or even inside it. When hydro-ureter is present it is not usual to see any change in the ureteric orifice on cystoscopy.

Stones may form in the bladder or in a diverticulum. When in the latter they are sometimes multiple. On X-ray the position of the opacity may suggest that it is outside the bladder.

A cystogram should always be carried out and the radiological appearances are often best seen when this is part of an excretion urography. It may, however, be necessary to fill the bladder with an opaque medium such as sodium iodide, and if in any doubt as to the position of a diverticulum or the number, oblique and lateral views should be taken. As a general rule the diverticulum is easily seen as a rounded or pear-like projection from the lateral wall of the bladder. The neck, formed by the thickened bladder muscle, will often show a well-marked gap between the diverticulum and the bladder. Occasionally two sacs open into the bladder through one orifice (Fig. 5.) A picture taken after micturition

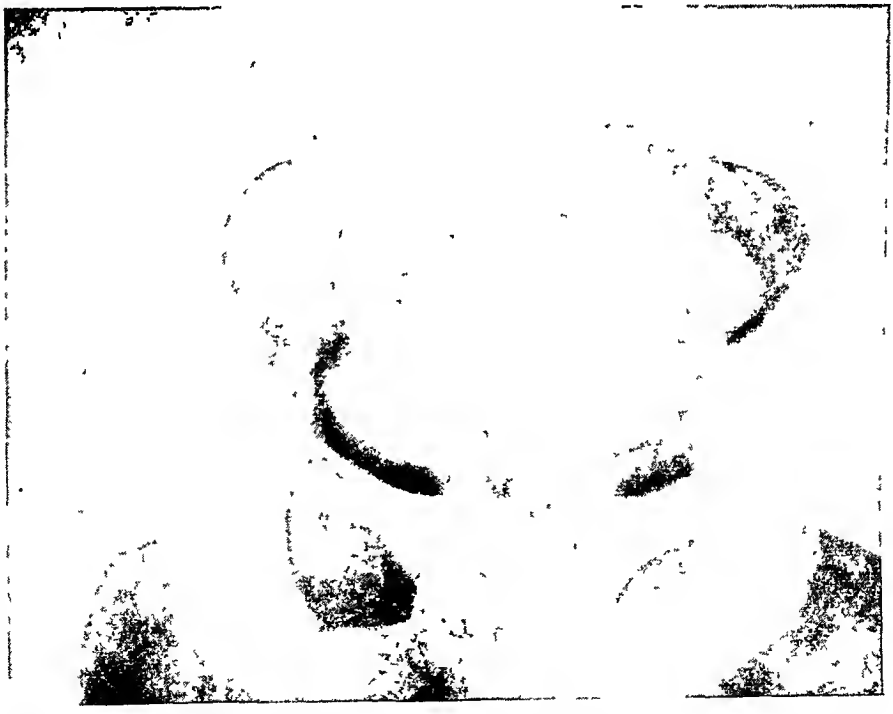


Fig 5. Two diverticula opening through one orifice

shows the true residual urine, and may show that the bladder has emptied into the diverticulum.

On cystogram the early stages of trabeculation may be seen, as a roughened irregular area on the otherwise smooth contour of the bladder. As the trabeculation increases, so also does the irregularity of the bladder contour.

If still in doubt, prior to operation, as to whether or not there is an obstruction at the internal meatus, the diagnosis can always be confirmed on opening the bladder. The internal meatus is found to be extremely narrow, very tight, and fails to admit the tip of a finger.

The cause of this condition has given rise to much discussion. There is no doubt that for such a severe degree of obstruction there is very little to be demonstrated in the way of an obstructive factor. All the earlier writers considered that the condition was due to fibrosis and it may be that chronic inflammation of the trigonal muscle or of the sphincter will lead to loss of contractility and failure of opening of the internal meatus. Histological examination of the wedge of tissue removed in this series has not shown fibrosis in any case, and in the large majority there is nothing but muscle tissue. (Figs. 6 and 7.) Occasionally, especially in the older group, there may be a little adenomatous tissue as well as muscle.

I believe, with Marion, that the obstruction is due to hypertrophy of muscle, probably analogous to congenital pyloric stenosis and cardiospasm. It is because of this, because of the age group and length of history, and because it does occur in infancy and childhood, that I believe that the condition is congenital. Obviously, if obstruction is very severe in infancy the child will not live, and many of the cases of bilateral hydronephrosis and hydro-ureter seen in childhood and adolescence are almost certainly due to this. In the patient who reaches adult life, obstruction may have been very slight at birth, but the obstructive factor is slowly progressive. At first the diverticulum or dilated ureters take up the back pressure, but if attention is not drawn to the condition on account of some complication, such as infection, eventually total retention—either acute or with overflow—results. It may be that a similar clinical condition can be acquired as a result of chronic prostatitis, or prostatic calculi. I believe this is rare however. Many cases have been considered to be due to a fibrous prostate and have been cured by removal of the prostate. I feel sure they would have responded just as well to a wedge resection or a simple prostotomy, and believe that the so-called fibrous prostate may be the normal gland in old age when hyperplasia has not occurred.

With regard to treatment, Guthrie suggested that leeches should be applied to the perineum to relieve the acute pain of the bladder spasm, and that a catheter should be worn. The wearing of the catheter was to continue for at least half-an-hour on retiring, during which time the patient had to change his position frequently in order to empty the urine from the various pouches. This is a very good observation to have made 120 years ago, without the advantages of endoscopic instruments or

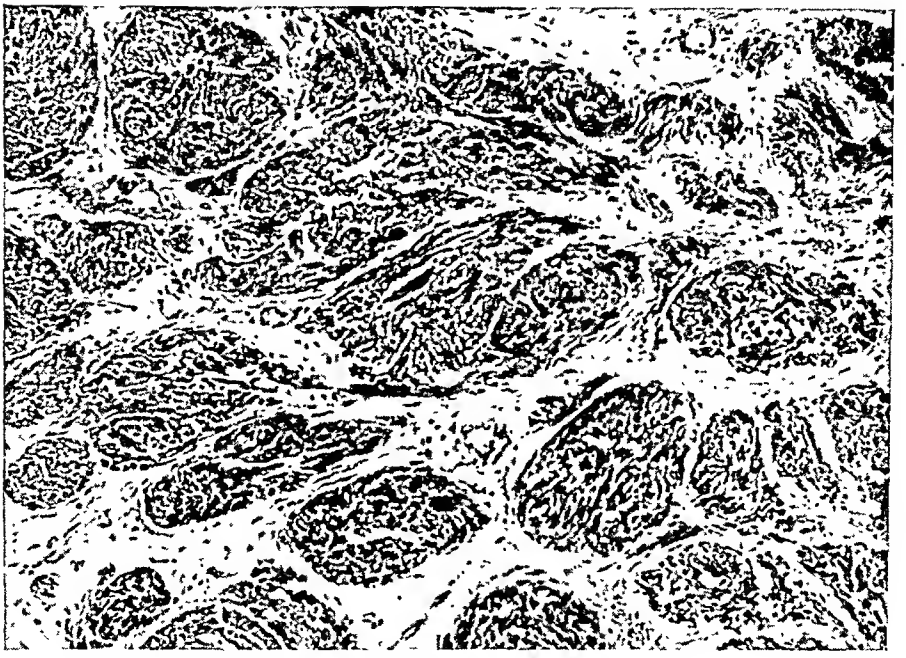


Fig. 6
Micro-photograph of section of bladder neck, showing bundles of muscle fibres.

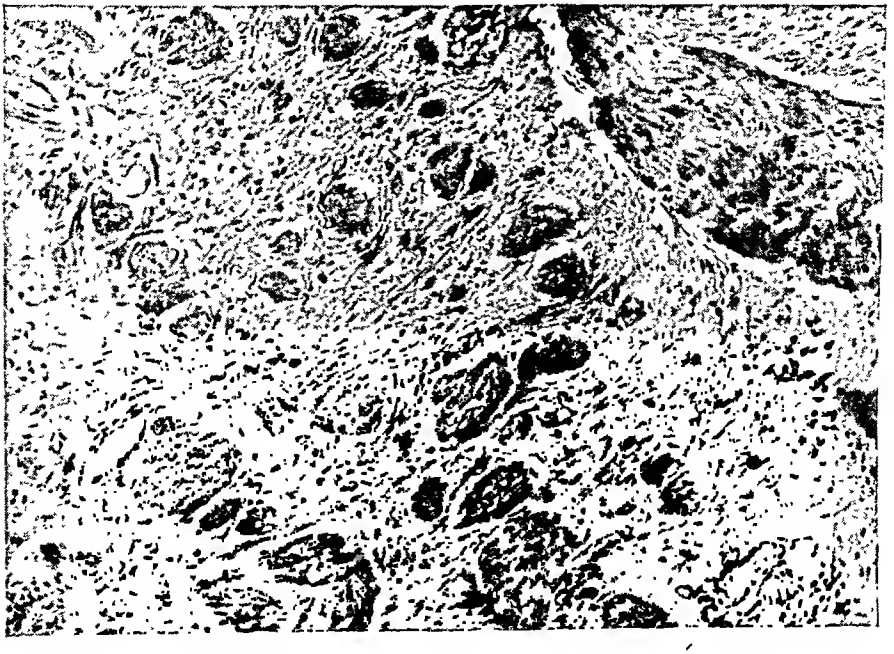


Fig. 7
Histological appearance in a wedge from a boy of seven years, showing bundles of muscle fibres.

X-rays now at our disposal. If this treatment were to fail he suggested dividing the bar at the posterior arc of the internal meatus, and designed a catheter containing a concealed knife which he apparently used on two patients. Mercier, several years later, employed an instrument rather like a lithotrite which crushed and cut at the same time, and in his hands its use was followed by considerable success. Young in 1912, introduced a punch for the treatment of the condition. The large series of cases he quotes were, of course, by no means all congenital: some being, undoubtedly, enlargement of the middle lobe of the prostate.

I believe that the congenital type in nearly every case has associated with it another factor; occasionally bilateral hydro-ureter, but in the large majority, diverticulum of the bladder. It is my practice to deal with the obstructive factor when the bladder is opened for removal of the diverticulum. Marion, in 1927, advised the complete extirpation of the internal meatus and sphincter. I think this is unnecessary, and so far have followed the late Swift Joly in removing a wedge from the posterior arc of the internal meatus. Even this is probably unnecessary and a simple incision or prostotomy as practised by F. J. F. Barrington may be sufficient to relieve the obstruction. This operation is analogous to the Ramsted in congenital pyloric stenosis. W. K. Irwin (1939) designed a clamp which he applies to the posterior arc and this enables him to cut without causing bleeding.

A diverticulum may be removed in one of four ways. If it is small and has not been the site of much infection it can usually be invaginated by picking up the lining with Aliss forceps, drawing it into the bladder, when it is cut off at the neck. Should this not be possible, the edge of the diverticulum is picked up in tissue forceps, an incision encircling the orifice is made, and the diverticulum gradually dissected out of its bed and drawn into the bladder. Care must be taken of the ureter and also of the vas deferens when this approach is adopted. All bleeding points must be picked up before the traction on the diverticulum has been released. In the large infected and adherent types neither of these two measures is practicable. The bladder is freed laterally, down to the sac. If the latter can also be mobilized, then it may be divided at the neck, the sac removed and the opening closed from outside. If it is impossible to effect mobilisation, in this way, the bladder must be divided down to the neck of the diverticulum, an encircling incision made round the orifice, and the whole dissected under direct vision. The bladder is drained either by a straight tube of the Marion type, or by a self-retaining tube, depending on the amount of bleeding. If the diverticulum is large and especially if the para-vesical space has been widely opened, a drain should always be left alongside the bladder for several days. The bladder is drained until bleeding ceases and then allowed to close.

When there is no diverticulum present, either because it has been removed at a previous operation, or because the obstruction has produced bilateral hydro-ureter, it is usually possible to relieve the

obstruction by endoscopic means, a wedge being removed with the resectoscope or cold punch.

It is interesting to note that if the diverticulum alone is removed, the obstruction will continue to show itself. This was pointed out by the late Swift Joly in 1923 and again by R. Ogier Ward. Either the bladder will fail to close and a fistula will result, or a bilateral hydro-ureter develops. (Figs. 8 (*a*) and 8 (*b*)). If, on the other hand, obstruction is removed but the diverticulum is not, then continuous infection, impossible to eradicate, will remain in the diverticulum on account of inadequate emptying. (Figs. 9 (*a*) and (*b*)). It may be that there will be no improvement on micturition, since the bladder empties into the diverticulum.

The results of treatment are on the whole satisfactory. Twenty-six cases, considered to be congenital bladder neck obstruction, have been treated. Of the 23 associated with diverticulum of the bladder, one patient, a case of Buerger's Disease, was treated by suprapubic drainage only. In the other 22 cases the diverticula were removed suprapubically, and in 16 a wedge excision of the bladder neck was done at that time. In six the obstruction was removed or relieved by resection of a small portion of tissue from the bladder neck using the McCarthy resectoscope. In two of these I failed to diagnose obstruction at the bladder neck prior to operation, and only did so when the suprapubic wound would not close. The other four were operated on in the first instance elsewhere, three presenting with suprapubic fistula, and the remaining case with acute retention of urine and bilateral hydro-ureter three months after diverticulectomy.

Two cases presented with retention and bilateral hydro-ureter; a boy of seven was treated by cystostomy and wedge excision, and the other case by resection.

The last patient was a man of 47, who, although he had neither diverticulum nor hydro-ureter, had 620 m.l. of residual urine and a 20 years history of difficult micturition. He was treated by resection, 2 gms. of tissue being removed; the residual urine was reduced to 50 m.l. and, like so many of the cases, he stated that he could not remember when he had had such a good urinary flow.

One patient died. He was suffering from myeloid leukæmia which was not diagnosed prior to operation. Two are still being drained suprapubically—the boy of seven and the man with Buerger's Disease. One remains infected and has not been relieved of his symptoms. One has had the residual urine reduced from 600 m.l. to 200 m.l., and feels so much better that he does not want any further intervention. The remaining 21 are very well, to all intents and purposes free from symptoms, with little or no residual urine.

In any patient who has an obstructive factor which is considered to be hypertrophy of the bladder neck, a careful search must be made for a diverticulum. Conversely, a patient with a diverticulum of the bladder or with bilateral hydro-ureter, unless proved otherwise should be considered

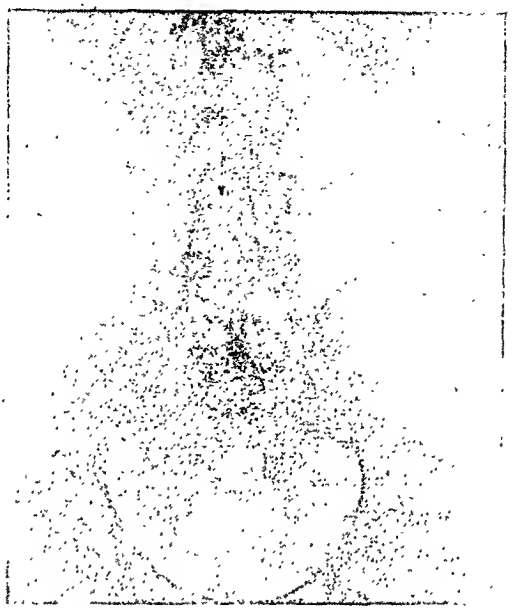


Fig. 8 (*a*) Excretion urography before removal of a diverticulum.

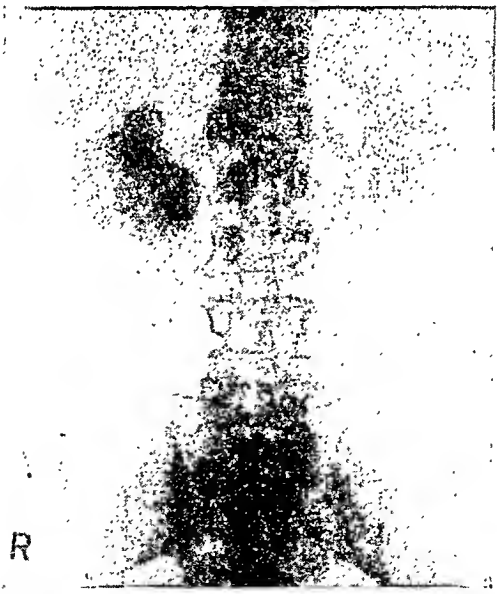



Fig. 8 (*b*) Excretion urography three months after removal of diverticulum without removal of obstruction, showing marked hydro-ureter and hydronephrosis.

Fig. 9 (*a*)

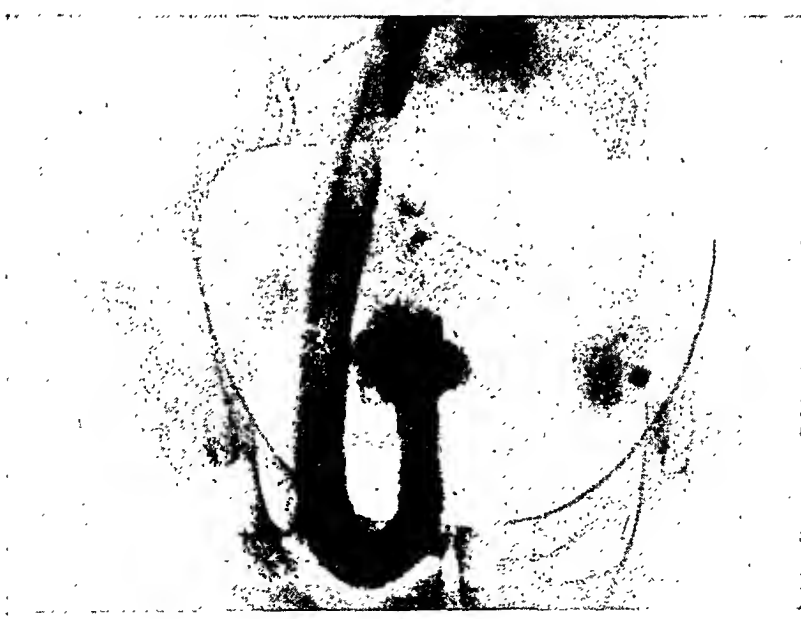


Fig. 9 (*b*)
Cystogram after suprapubic cystostomy.
(*a*) Bladder full and tube spiggotted.
(*b*) Spiggot released showing that the diverticula have not drained.

to have bladder-neck obstruction. If incorrectly treated, the patient often a young man, will suffer from marked frequency of micturition, from pain, from nocturnal eneuresis, or from a permanent supra-pubic fistula.

On the other hand, if the correct diagnosis is made, the treatment is comparatively simple and for so severe and lethal a disease, the results are very satisfactory.

## REFERENCES

BARRINGTON, F. J. F. *Personal Communication.*
BUGBEE, H. G., WOLLSTEIN, M. (1923) *J. Urol.* **10**, 477.
CAMPBELL, M. (1937) *Pediatric Urology*, New York, The Macmillan Co.
CHETWOOD, C. H. (1913) *J. Amer. Med. Ass.* **60**, 265.
FULLER. *Quoted by Young.*
GUTHRIE, G. I. (1834) *London Medical and Surgical Journal* **4**, 459.
(1834) *On the Anatomy and Diseases of the Neck of the Bladder.* London.
IRWIN, W. K. (1939) *Brit. J. Surg.* **26**, 764.
JOLY, J. S. (1923) *Lancet* **2**, 445.
KEYES. *Quoted by Chetwood.*
MARION, G. (1927) *J. Urol. méd. chir.* **23**, 97.
MERCIER, LOUIS AUGUSTE (1933) *History of Urology*, Williams and Wilkins, Baltimore, **2**, p. 93.
WARD, R. OGIER (1925) *Brit. J. Surg.* **13**, 144.
(1938) *Brit. J. Surg.* **25**, 790.
YOUNG, H. H. (1913) *J. Amer. Med. Ass.* **60**, 253.
——— and MCKAY, R. W. (1929) *Surg. Gynec. Obstet.* **48**, 509-535.

## SAYINGS OF THE GREAT

"Our duty is not to see what lies dimly at a distance, but to do what lies clearly at hand."—*Carlyle.* (Contributed by Ronald W. Raven, O.B.E., F.R.C.S.)

"Beware how you take away hope from any human being. . . . It is the height of cruelty and the extreme of impertinence to tell your patient he must die, except that you are sure he wishes to know it, or that there is some particular cause for his knowing it."—*Oliver Wendell Holmes.* (Contributed by C. Noon, O.B.E., F.R.C.S.)

"The great use of life is to spend it for something that will outlast it."—*William James.* (Contributed by C. Allan Birch, F.R.C.P.)

"Experience is of no ethical value. It is merely the name men give to their mistakes."—*Oscar Wilde.* (Contributed by C. Allan Birch, F.R.C.P.)

"The true aim of the teacher should be to impart an appreciation of method and not a knowledge of facts."—*Karl Pearson.* (Contributed by C. Allan Birch, F.R.C.P.)

"The most interesting thing in the world is something growing on the other side of a high wall."—*Victor Hugo.* (Contributed by C. Allan Birch, F.R.C.P.)

*Note.*—Contributions are invited.

# THE PROBLEM OF CLOSED HEAD INJURY

Lecture delivered at the Royal College of Surgeons of England

on

8th October, 1947

by

G. F. Rowbotham, B.Sc., F.R.C.S.

Department of Neurological Surgery, Newcastle General Hospital

MY PRIMARY INTENTION in this paper is to state as clearly as possible what the main problems of the closed head injury really are. It is my belief that there is too great a tendency to jumble the physics of injury with the pathology of acute cerebral trauma and also to confuse the general pathological complex with the neuro-physiology of so-called concussion.

## THE PHYSICS OF INJURY TO THE BRAIN

A. *A patient may fall or may be thrown and brought to rest:*

(*a*) by some part of his body, other than his head, coming into contact with a distant object—for example—the ground.

or

(*b*) by his head hitting the ground. ([1] Fig. 1.)

(i) and crushed by the weight of the body when the injuring force passes through the centre of gravity and the spino-occipital attachment. ([2] Fig. 1.)

or

(ii) and set into rotation when the head is struck away from the centre line of force. ([3] Fig. 1.)

B. *The head may be struck by a large object when the patient is stationary:*

(*a*) and knocked away and set into rotation. ([4] Fig. I.)

or

(*b*) crushed against the spinal column. ([5] Fig. 1.)

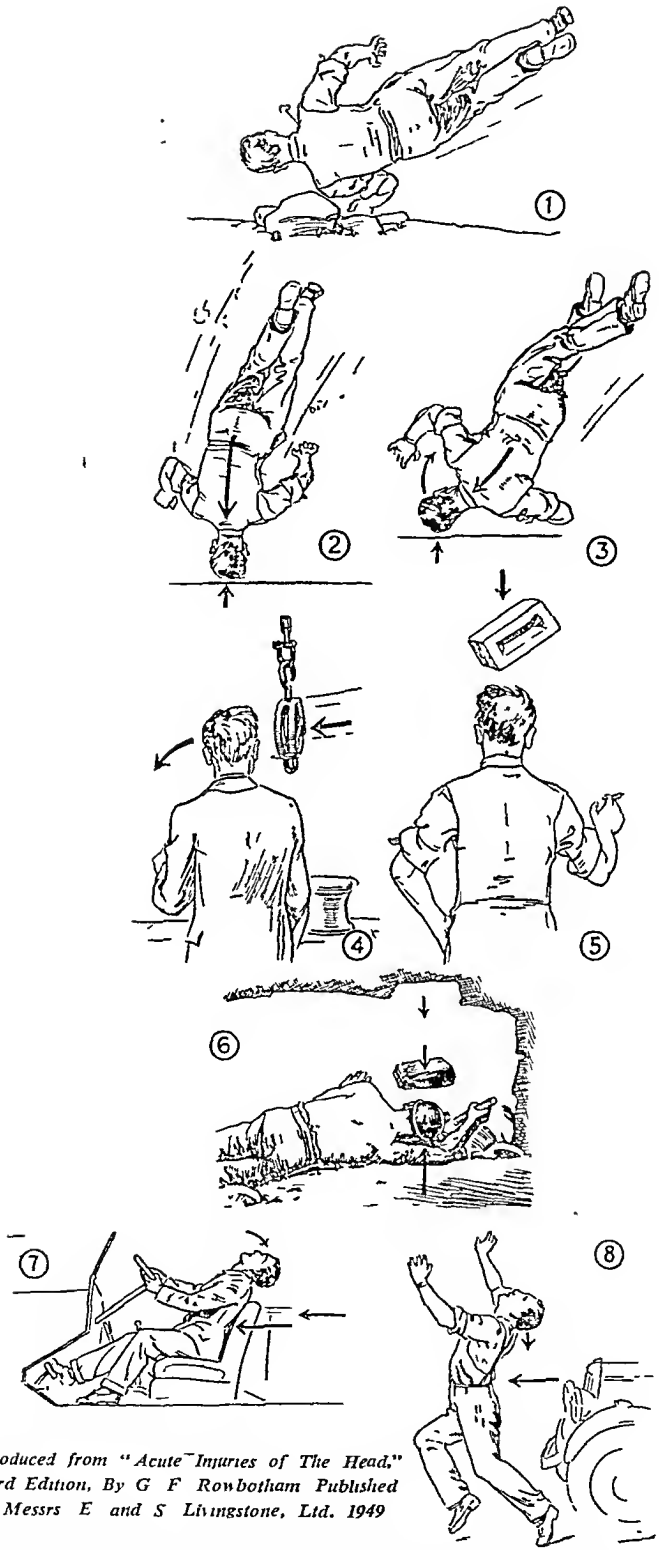
or

(*c*) crushed between two large external objects. ([6] Fig. 1.)

C. *The patient may be struck in the back and his head thrown into violent rotation.* ([7] and [8] Fig. 1.)

In many cases of accident the head is subjected to a combination of different injuries. For example, a man may fall from a height and on the way to the ground might strike his head against several objects, each blow setting the head into violent rotation about a different axis. Also, the head may not only be rotated but may finally be crushed.

The forces of acceleration and deceleration act similarly and so a man's brain may be injured at the beginning or end of a throw. It is true that, owing to the conditions of civilised life, injuries to the brain are commonly brought about as the result of the forces of acceleration and deceleration,




*Reproduced from "Acute Injuries of The Head," Third Edition, By G F Rowbotham Published by Messrs E and S Livingstone, Ltd. 1949*

Fig 1. The head is subjected to violences that are variable in magnitude, direction and area of application.

for the reason that human beings happen frequently to ride in fast-travelling motor-cars which come into collision.

None the less, there is no special type of concussion that can be attributed to the forces of acceleration. The immediate cause of cerebral injury is essentially distortion of the brain and it is of no pathological import how this distortion is brought about. If a word were needed it would be better to speak of distortion-concussion, rather than of acceleration-concussion, as there is a tendency now to do. It is best, however, to remember that concussion is brought about by distortion. The critical speeds of acceleration, that initiate sufficient distortion to bring about cerebral injury, differ not only in different heads but also along different axes in the same head. It is of importance, from the medico-legal point of view, to know that it is impossible from the nature of cerebral injuries to reconstruct precisely the physics of a violence.

To summarize, practically all the physics of closed cerebral injury resolves itself into distortion ; this distortion can be initiated by all kinds of force, such as rotation, sliding, shaking and squashing and these in their turn may be brought into action by all kinds of accident. My advice to you, should you contemplate research in cerebral injuries, is not to devote your genius to devising newer types of violence that can be directed to the head.

Finally, may I stress that the physics of cerebral injury is a subject in itself and quite distinct from the problem of pathology, diagnosis and treatment. Its main importance is that the conditions are such, that practically the whole brain is subject to injury in most kinds of accident.

## THE PATHOLOGY OF INJURIES TO THE BRAIN

*The Three Primary Pathological States :*

(i) Contusion.
(ii) Concussion.
(iii) Diffuse Neuronal Injury.

*Secondary Pathological Developments.* (Fig. 2-5.)

(*a*) Shock.
(*b*) Intracranial hæmorrhage—extradural
—subdural
—subarachnoid
—intracerebral
—intraventricular
(*c*) Oedema—generalised
—local
(*d*) Hydrocephalus—internal
—external
(*e*) Herniations of the brain.
(*f*) Infections which enter the cranial cavity through the middle ear.
(*g*) Epilepsy resulting from the trauma.
(*h*) Loss of blood from superficial wounds.
(*i*) General effects of injuries to other organs.
(*j*) Fatty emboli.

Fig. 2. A large subarachnoid hæmatoma.

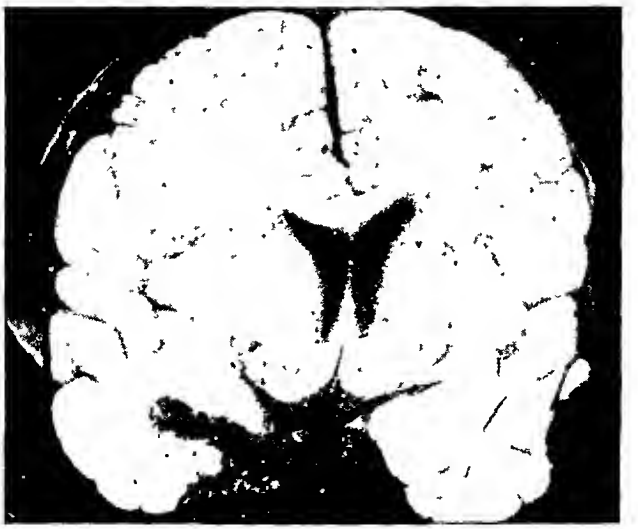


Fig. 3. Subdural hæmorrhage displacing the ventricles.

Fig. 4. Even a thin layer of extradural blood can jeopardise a patient's chances of recovery in cases of intrinsic injuries that in themselves are not lethal.

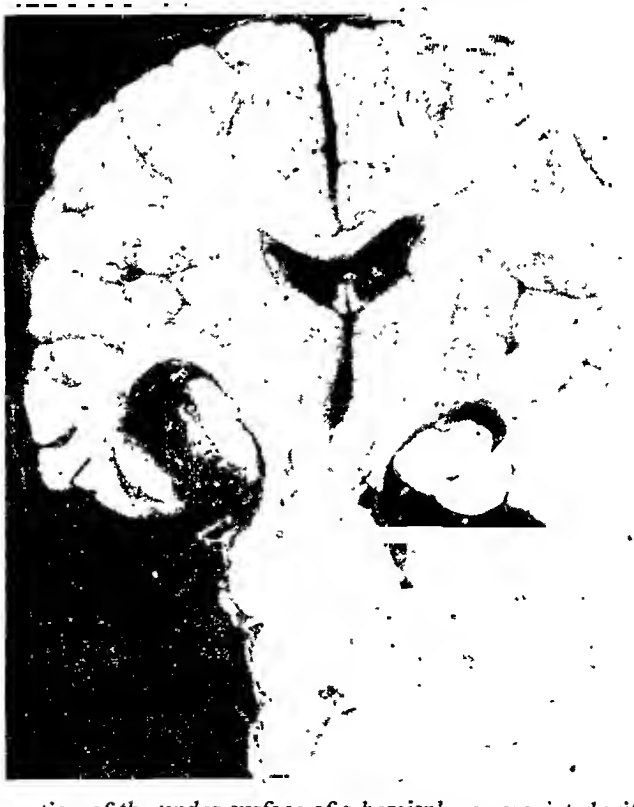


Fig. 5. A laceration of the under-surface of a hemisphere associated with an extensive subdural hæmorrhage.

*Diffuse Neuronal Injury.* First let us consider the problem of diffuse neuronal injuries. The term concussion has no pathological implication ; by agreement, it means purely and simply impairment of consciousness resulting from trauma. The term commotio cerebri has, on the other hand, an ambiguous pathological implication. It suggests that a number of cells of the brain, of unknown localisation, have received a type of injury that cannot be demonstrated by histological examinations. Possibly, when speaking in terms of pathology it would be best to discard the term commotio cerebri and speak of diffuse neuronal injury. In considering diffuse neuronal injury there are two questions to be asked and answered, and these are :

1. What is the nature of the injury to the neurones ?
2. What part of the brain has been injured to account for the symptoms observed clinically ?

*The Nature of Neuronal Injury.* If we are to get any conception of the nature of an injury to a single neurone we must of necessity symbolise, because the exact structure of a neurone is not known. Moreover, there is no method yet available that will demonstrate anything but a complete destruction or gross change in a nerve cell. From general principles we can conjecture what the nature of a neuronal injury is likely to be :

(*a*) A synapse may be slightly disturbed or completely disrupted.
(*b*) A cell membrane may be punctured or torn to shreds.
(*c*) Intracellular bodies may be altered in their relationships to one another, or an intracellular body itself may be broken up.
(*d*) The nature of an injury obviously will determine whether a cell is killed and, if not, how long it remains paralysed or in a state of dysfunction.

This problem of the exact nature of an injury to a brain cell is one that must be solved if a real advance is to be made in the study of concussion. Indeed, this is a problem that should be unceasingly brought before the notice of people in the College interested in research.

*What part of the brain has been injured to account for the symptoms observed clinically ?* From some neurological signs it is possible to say with reasonable certainty that a known and circumscribed area of the brain has been injured. For example, from a hemiplegia that has developed through the stages of convulsive movements, spastic and flaccid paralysis, a diagnosis can be made with certainty that the opposite motor cortex has been injured. Moreover, certain postures indicate that damage has occurred at certain levels of the brain stem. On the other hand the localisation of unconsciousness is not known and this is unfortunate because unconsciousness is one of the outstanding clinical features of a head injury. It is obvious, on clinical and experimental grounds, that a severe contusion of the brain stem will lead to coma. This, however, does not mean that every degree of unconsciousness can be attributed to brain-stem damage.

My own impression is, that recovery from unconsciousness reveals the recovery of brain function, from the low levels upwards, rather than the gradual recovery of a so-called centre of consciousness.

My suggestion is, that deep coma should be regarded as a sign of brain-stem injury : semi-coma, as a sign of bilateral hemispheral paralysis ; and confusion, as impairment of function of the frontal lobes of the brain. That semi-coma is a sign of hemispheral paralysis seems to me to be established on the grounds that in this degree of unconsciousness all the brain-stem reflexes are active, whereas those of the hemispheres are in abeyance. For example, if a light be shone into the eyes of a semi-comatose patient his pupils will react actively ; this is a brain-stem neural mechanism. On the other hand, if a frightening object be brought before the eyes of a semi-comatose patient he shows no evidence of fear and makes no effort to move away to safety. Reactions of fear to a frightening object depends on a hemispheral mechanism.

To summarize, coma indicates brain-stem damage ; semi-coma, hemispheral paralysis ; and confusion, dysfunction of the frontal lobes.

## THE PROBLEM OF DIAGNOSIS AND TREATMENT

Let us now consider the general pathological complex and view it from the angle of diagnosis and treatment. It is obvious that the primary intrinsic injuries and the secondary pathological developments act, and interact, affecting the functioning of the central nervous system to produce the final clinical picture. Let us, for example, take a severe brain-stem contusion. In this case the effect of a primary injury will be the dominant feature. The injury will render the patient immediately unconscious and by the time he is examined he will almost certainly be in coma. On the other hand, let us consider the case where the primary injury has been minimal but in which a large surface hæmorrhage slowly accumulates. The patient will be a little more than momentarily dazed by his accident but will later slide slowly into unconsciousness, the dominant feature in this case being the latent interval. Between these two extremes, innumerable combinations and degrees of the various pathological factors can occur to produce innumerable differences in the clinical picture. Indeed, the problem is so difficult and confused that I believe it is justifiable to symbolise in an endeavour to gain understanding and clarity.

Let us represent the primary intrinsic injury by an inner circle and divide it into three sectors to represent the special injuries of laceration, contusion and diffuse neuronal injury. Let us represent the secondary pathological manifestations by a large outer circle encircling the smaller inner circle. This outer circle may be divided into sectors to represent the secondary pathological manifestations such as shock and surface hæmorrhage. (Figs. 6, 7 and 8.)

Let us reproduce each sector in colour rather than in word labels and let us spin the model on a pin passed through its centre. When the model spins the colours will fuse, the final tint depending on the colours

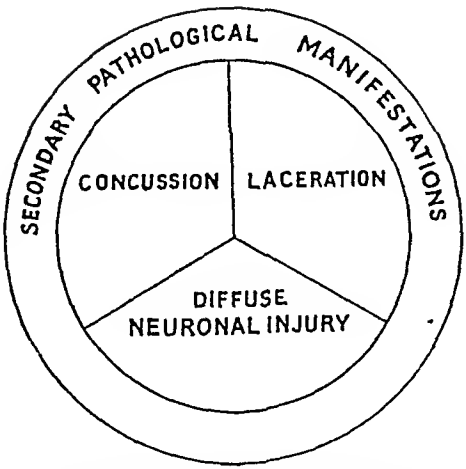



Fig. 6. When the intrinsic injury is overwhelmingly severe, the secondary pathological manifestations are not important.

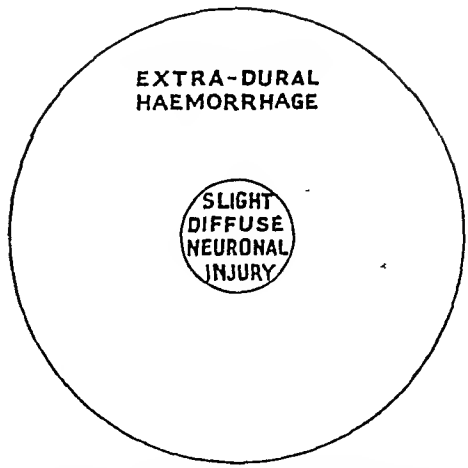



Fig. 7. In favourable cases of extra-dural hæmorrhage the intrinsic injury is minimal.

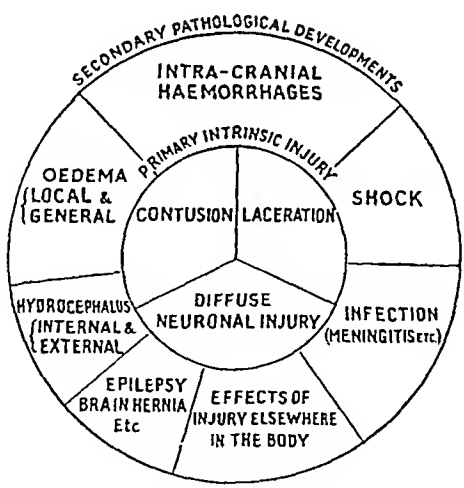



Fig. 8. A typical example of intrinsic and secondary pathological lesion.

*Figs. 6, 7 and 8 reproduced from "Acute Injuries of The Head," Third Edition, By G. F. Rowbotham. Published by Messrs. E. and S. Livingstone, Ltd. 1949.*

used in each sector, on the depth of each colour and on the relative breadth of each sector, this breadth representing the importance or dominance of a single pathological factor.

To continue with the symbolisation, the problem for the clinician is to slow down the rotation of the model when the individual colours of each sector will become clear and can be interpreted in terms of pathology. What I am trying to stress and illustrate is that the final clinical picture of a head injury is the result of a complex integration of various pathological factors. Until this is realised and until each factor can be taken out and analysed separately, no logical effort can be made at diagnosis.

Let us, for example, consider the state of contusion. A contusion, by definition, is a molecular loss of continuity. The results of a cerebral contusion will depend on the length, breadth and depth of the area concerned ; on whether the contusion is single or multiple and more particularly on which part of the brain the contusion affects. A contusion of the surfaces of a hemisphere is relatively unimportant, whereas a contusion of the hypothalamus is likely to be fatal.

Then, for example, let us consider a single factor from the secondary pathological manifestations. Let us select a subarachnoid hæmorrhage, which happens to be a very common accompaniment of any head injury. What are the effects of a subarachnoid hæmorrhage acting alone ? We happen to know the answer to this question by looking to general medicine, where spontaneous subarachnoid hæmorrhages occur quite frequently. The outstanding features in such cases are shock, pain, restlessness and drowsiness. What effect, then, can subarachnoid hæmorrhage have on a patient who is already struggling against the effects, say, of contusion and œdema of both frontal lobes of the brain ?

Often I am asked what can be done for concussion, the question implying a diffuse neuronal injury. Possibly very little. On the other hand, what can be done for a closed head injury is of immense importance and one has only to consult the long list of secondary pathological manifestations to appreciate this. Indeed, it is my experience, based on a long series of post-mortems, that the human being very rarely indeed dies from a diffuse neuronal injury unaccompanied by frank secondary pathological manifestations. My object in mentioning the fact is that I believe that very many more people who die from head injury can be saved ; certainly illnesses can be curtailed and sequels minimised.

I would like to encourage far more people along this fascinating pathway of the problems of cerebral trauma. Certainly for the proper understanding of cerebral injuries a basic neurological knowledge is essential. None the less, however, it is a subject that is well within the scope of the general surgeon.

---

I would like to thank my secretary, Miss Norma Harvey, for her help in the preparation of this work.

# THE FEMALE BREAST AND ITS DEVELOPMENT

Lecture delivered at the Royal College of Surgeons of England
on
15th December, 1948
by

C. M. West, M.C., D.Sc., M.B., B.Ch.
Department of Anatomy, University College, Cardiff

THE FEMALE BREAST must have been of interest to us all from our earliest days. For some it has retained an interest into later life and it has been a theme for poets, artists and sculptors ever since Art began.

The term breast is sometimes used as synonymous with mammary gland, which is incorrect, but since, from a functional point of view, the mammary gland is the most important part of the breast I propose to deal with it first, and to consider its developmental history from its earliest stage to its senile condition.

In man the mammary apparatus is foreshadowed by the "milk-streak," a wide area of ectodermal thickening with a condensation of the underlying mesoderm that extends from axilla to groin, and of which the cranial part becomes raised to form the "milk line" (Bresslau, 1920). Though a milk streak has been identified at the 7mm. stage, it is not easy to recognise it so early, but at 11mm. or 12mm., that is, in the sixth week, it can be clearly seen looking, rather, as if the skin of the trunk had been pulled up as one pulls up a fold of a loosely fitting coat or a shirt on lifting the arm. At such a stage an additional thickening, the milk line, can be seen raised up on the surface of the streak.

In an embryo of the seventh week, of 18·8mm. C.R. length, though the mammary area cannot be readily seen in surface view sagittal sections show a series of nodules or thickenings of the ectoderm stretching in a line along the ventral thoracic wall. At this stage the ectoderm is composed of a superficial layer of flattened cells and a deeper layer of cubical cells. In the deeper layer the nuclei occupy the superficial pole of the cells so that the deeper half of the cell appears clear, and the ectoderm as a whole seems to be separated by a clear zone from the underlying mesoderm. As we shall see later this forms a useful guide in distinguishing ectodermal and mesodermal derivatives.

Figure 1 shows a sagittal section through the left side of the thorax of an 18·8mm. human embryo. The ribs are cut transversely and as the arms were folded across the chest a portion of one forearm, cut transversely, also appears in the section. On the chest wall five thickenings, some larger than others, can be seen, and Figure 2 shows two of them at a higher magnification. It shows the two layers of the ectoderm mentioned above and one can see that it is the deeper of the two that is involved in the thickening and that a cleft-like space intervenes between the two

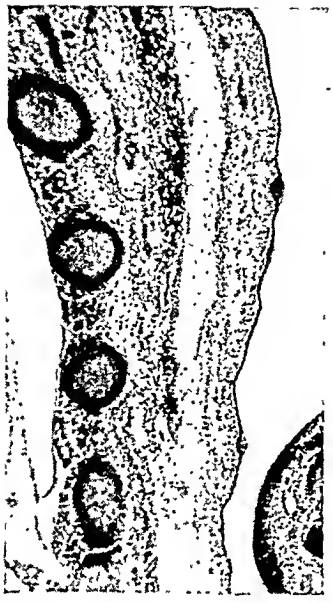


Fig. 1. Sagittal section of embryo 18.8mm. C.R., showing ectodermal mammary thickenings × 42.

Fig. 2. Two of the thickenings shown in Fig. 1 × 200.

Fig. 3. The definite mammary rudiment of embryo shown in Fig. 1 × 42.

layers. It shows, too, the clear basal ends of the cells of the deep layer overlying the mesoderm. This deep layer is the future stratum germinativum of the epidermis. The larger of the two thickenings shown in Fig. 2 is about six cells thick. It is not, however, the rudiment of the definite

left mammary gland of this embryo, but this appears in another section shown in Figure 3, which is 370μ further from the middle line than the rudiments shown in Figures 1 and 2. The ectodermal thickening that will form the definitive mammary gland is much more extensive than the others, which normally degenerate. Figure 3 shows again the individuality of the two layers of the ectoderm and it shows well the clear zone that marks the boundary of the ectoderm. Bearing this boundary in mind it is evident that the mesoderm adjacent to the ectodermal thickening is itself condensed and forms a cup filled with the ectodermal cells. Subjacent to the cup also the mesoderm is condensed. It is from this condensation that the muscular and supporting connective tissue of the mammary gland will be derived, while the secretory portion of the gland will be derived from the ectodermal thickening that fills the mesodermal cup.

Persistence of the discrete thickenings in the mammary line seen in Figure 1 results in the development of a series of mammary glands, their final disposition depending upon which of the original thickenings does persist and grow. Among the various mammals it may be all or only the pectoral, or inguinal, that persist, or both pectoral and inguinal may persist with a gap in the middle region.

In man, normally, the pectoral thickening persists on each side to form the definitive gland. Cases of supernumerary glands are not uncommon and when such glands do occur they are found, as would be expected, along a line extending from axilla to groin. But, since the mammary gland is, as we shall see later, a modified sweat gland, there is no apparent reason why supernumerary glands should not occur anywhere on the body, and they have, indeed, been found in a great variety of situations (see Patten, 1947, Fig. 141), and in both male and female.

While looking through my embryological material in preparing this lecture I came across a female fœtus, 125mm. long, of about the fourth month which showed beautifully a supernumerary mammary gland on the right side. By comparing the two sides of the body it became clear that the supernumerary gland was below the normal one. Each mammary gland appeared in the intact fœtus as a circular, slightly depressed area 3mm. in diameter, inside which was a slightly raised area 1mm. in diameter. The whole area stood out sharply from the adjacent skin by its complete hairlessness. Over other parts of the body the hair showed particularly well. The normal and the supernumerary gland were cut out and embedded in one block and sectioned serially at 10μ.

Figure 4 is a photograph at low magnification of a section through the supernumerary gland. It shows the absence of hair follicles over an area in the middle of which is the ectodermal thickening of the gland. At this stage the epithelium is beginning to be shed and the epidermis is now several layers thick, but, as can be seen with higher magnification (Figure 5, which is a section through the normal gland) it is still the cubical deep layer with its superficially placed nuclei that lines the mesodermal cup.

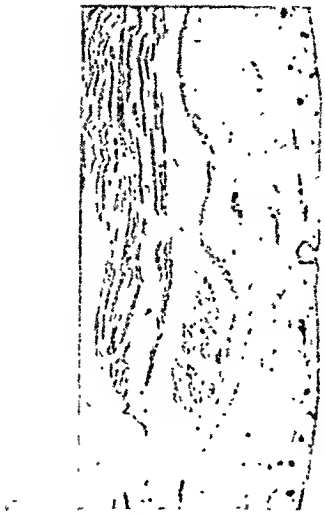


Fig. 4. Sagittal section of supernumerary rudiment in fœtus of 125mm. C.R. × 12.

Fig. 5. Definitive mammary rudiment of same fœtus as Fig. 4 × 42.

It seems that in this specimen both ectodermal ingrowths would have persisted and the child would have had a supernumerary gland and nipple on the right side.

Figure 5 shows the absence of hair follicles adjacent to the glandular area but there is a great development of blood vessels, which is another characteristic of the mammary area. It can be seen too that the peripheral edge of the ingrowth is not as smooth as it was, but is beginning to give off little sprouts. These are the earliest signs of the future lactiferous ducts. They grow into the underlying mesoderm which helps to form the involuntary muscle that is characteristic of later stages.

The further development of the mammary gland consists of an enlargement and branching of the original sprouts so that there is ultimately formed a complicated mass of glandular tissue, composed of lobes, lobules and alveoli or acini. The differentiation of the alveoli is a

prominent feature of the later stages of pregnancy but it is not certain how far alveolar development goes in the virgin.

It was William Cruikshank, assistant to William Hunter in the Great Windmill Street Dissecting School who, in 1790, described the acini as " small vesicles like Florence flasks in miniature " (see Todd, 1847, p. 245), and he demonstrated them to John Hunter.

With regard to the actual secretory process the mammary gland belongs to the group of apocrine glands, those in which secretion involves partial but not complete destruction of the cells. This is one of the characters that allies the mammary gland to the sweat glands rather than the sebaceous. Fat globules can be seen to accumulate in the part of the cells of the alveolar epithelium that lies next the lumen of the alveolus, and this part of the cell then becomes pinched off so as to lie free in the lumen as the milk globules.

The general arrangement of the ducts, lobes and lobules of the mammary gland can be clearly demonstrated by rendering them opaque with thorotrast and then taking a radiograph, as was done by Hicken (1937). There is no communication between the different lobes, each remains distinct and has its own duct which opens on the summit of the nipple. As they lie within the nipple the ducts have only a very small lumen, but beneath the areola their diameter is much increased over a short distance so that elliptical reservoirs are formed. It was suggested by Sir Astley Cooper (1840, p. 55) that: " the use of these reservoirs is to supply the immediate wants of the child when it is first applied to the breasts, so that it shall not be disappointed, but be induced to proceed with sucking until the *draught* be produced." By the *draught* he means (p. 129): " a sudden rush of blood to the gland, during which the milk is so abundantly secreted, that if the nipple be not immediately caught by the child, the milk escapes from it, and the child when it receives the nipple is almost choked by the rapid and abundant flow of the fluid; if it lets go its hold, the milk spurts into the infant's eyes. Even the sight of the child will produce this draught or sudden rush of blood and copious supply of milk, as the thought and sight of food occasions an abundant secretion of the saliva."

The breast, as opposed to the mammary gland, begins its development at puberty, when, under the influence of ovarian estrogenic hormones there is a rapid and for some years continuous growth. In the adult the upper and lower surfaces of the breast are not symmetrical, for while the upper is directly continuous with the surface of the thoracic wall the lower forms a sharp angle with it, the breast having the appearance of having sagged, as indeed it does later. As pointed out by Astley Cooper two factors are responsible for this adult condition, in which the breast is thicker along its lower and outer borders than elsewhere; one is that there is a greater thickness, or folding over, of the edge of the mammary gland and the second is the greater accumulation of fat along the lower and lateral margin of the breast. In this way,

as Astley Cooper says, there is formed a convenient cushion on which the cheek of the child may repose while sucking. In this connexion it should be noticed that the breast and the nipple look forwards, upwards and outwards—again for the convenience of both child and mother. Though this asymmetry of upper and lower surfaces is characteristic of the adult breast there is a transient stage in late puberty when the breast though well developed is symmetrical, its upper and lower surfaces forming almost a right angle with each other.

In pregnancy the breast increases greatly in size due to growth of the mammary gland, and the growth may be such as to give rise to cicatrices like the striæ gravidarum of the abdominal wall, especially in women in whom, before pregnancy, the breasts were particularly small. After lactation and in old age the sagging of the breast becomes more marked (see Patten, 1947, Fig. 139, for different stages), but there is some racial variation in this. The breasts tend to be more dependent in coloured than in white women, and among primitive peoples such as the Bushman and the Veddah the nipple may reach below the level of the elbow.

The main factor, at least until pregnancy, responsible for the shape of the breast is fat. Frazer (1931, p. 460) has shown that fat begins to be deposited during the fourth month in cells of the subcutaneous region, but it is conspicuously absent from the cells immediately beneath the mammary rudiment. The outgrowths to form the lactiferous ducts make use of this fat-free gap on their way into the underlying mesoderm, and thus their subsequent growth and expansion takes place deep to the fat that has been laid down in the subcutaneous tissue. In this way it comes about that the order of the structures through which one passes in making a section of the adult breast is skin, fat, mammary gland, deep fascia. The mammary gland is, in fact, essentially in the plane of the superficial fascia. The arrangement of the fat did not escape the attention of Sir Astley Cooper and he has some interesting things to say about it. Thus, on p. 71: "Nature for several reasons has abundantly supplied this organ with adipose matter. (1) To preserve the contour; (2) to regulate the temperature of the gland under exposure, whether from the poverty which precludes the possession of proper covering, or the caprices of fashion, which forbid its being worn; (3) to allow the breast to float in an oily fluid; (4) to defend it from heavy blows." Later he refers to the "thick cushion of fat placed under the skin, which enables the women of the lower class to bear the very severe blows which they often receive in their drunken pugilistic contests."

It is in association with the fat of the breast that Sir Astley Cooper has won eponymous fame, for it is through the agency of the *Ligaments of Cooper* that the fat is loculated and the breast supported.

If one makes a vertical or horizontal section through the breast the fat can to a great extent be cleanly shelled out from the spaces it occupies, thus leaving the walls of the spaces behind. The walls of these spaces are the ligaments of Cooper, or, as he called them, the *ligamenta suspensoria*.

He gives several good illustrations showing how these bands of fibrous tissue are continuous among the glandular tissue of the breast from the fascia covering the pectoralis major to the skin. Since the pectoral fascia is fixed these ligaments do have some suspensory function. This fibrous tissue is continued into the nipple also and " is the chief defence from those injuries and violences which might tear off the mammilla from the gland."

Among the changes in the breast associated with pregnancy some of the most striking are those that affect the areola. These changes have been well described and beautifully illustrated by Montgomery (1837) in his classical account of the signs and symptoms of pregnancy. Montgomery was Physician to Sir Patrick Dun's Hospital in Dublin, and Professor of Midwifery in the King and Queen's College of Physicians in Ireland.

Even by the end of the second month the areola has become much darker than in the virgin state, and this increase in pigmentation continues throughout pregnancy until by the ninth month the areola may be almost as dark in colour as the skin of a negro. Montgomery regarded this areolar pigmentation as " one of the most certain external indications of pregnancy."

Montgomery's name is associated in particular with the cutaneous glands of the areola. There is some confusion about these glands for they are referred to as sebaceous, sudoriferous, accessory mammary glands, Montgomery's glands or merely cutaneous glands. By their enlargement in pregnancy they give rise to small elevations of the skin known as the *tubercles of Montgomery*. It seems doubtful, however, on what grounds Montgomery's name has come to be associated with these glands and tubercles.

Montgomery, himself, refers to " the integument being raised and in a state of turgescence " in pregnancy and he states (p. 59) that " the little glandular follicles or tubercles, as they are called by Morgagni, are bedewed with a secretion sufficient to damp and colour the woman's inner dress." The following paragraph occurs on p. 61 : " The surface of the areola, especially that part of it that lies more immediately around the base of the nipple, is studded over and rendered unequal by the prominence of the glandular follicles, varying from 12 to 20 in number." These words might be sufficient to give him eponymous fame were it not for the following footnote relative to the passage quoted : " These follicles though considered by many as merely sebaceous glands, have really a much more important character ; now it appears that these areolar tubercles are intimately connected with the lactiferous tubes, some of which can be traced into them and opening on their summit, so that in a pregnant woman a sero-lactescent fluid may be often distinctly perceived issuing from them, and in nurses they have been observed to pour forth drops of perfect milk (Morgagni). Each of these follicles

is furnished with very small sebaceous glands (Meckel)." It is thus not easy to decide how much of these observations is original.

Astley Cooper in his work published three years after the appearance of that by Montgomery does not mention the latter by name, but in speaking of the areola he says (p. 43): "At the base of the nipple, and again upon the surface of the areola, numerous tubercles appear in the skin; often they are placed upon the circumference of the areola where it joins the smooth skin. In these there are orifices very visible to the naked eye. The orifices vary in number from one to five. The tubercles perform three offices: first, they discharge from their little openings a lubricating secretion; secondly, they add to the firmness of the adhesion of the child's lips; and thirdly, they give greater sensitivity to the areola, and sympathetically excite a larger secretion from the mammary glands." He then mentions that Meckel and Morgagni thought they were connected with lactiferous tubes; that the glands are more evolved nearer the nipple. "In lactation they pour out a fluid which is coagulated by alcohol and its appearance is like white of egg. It has a tendency to lessen that excoriation which, when it does occur, renders suckling almost an agony."

It almost appears from the above that it is the name of Cooper, Meckel or Morgagni that should be associated with these tubercles rather than that of Montgomery, and indeed the name *tubercula Morgagni* is sometimes given to the elevations caused by the areolar glands. The truth seems to be that there are two sets of glands—those close to the nipple which are the glands of Montgomery and those nearer its circumference which are the glands of Morgagni. And yet it would surely be those that are nearer to the nipple from which milk might be expected to appear, as Morgagni is stated to have observed.

Maclise (1856, commenting on Pl. X and XI) is quite clear in his statement: "The tubercules of the areola mark the graduated transition between the sudoriferous and lactiferous glands. The tubercles are lactiferous and they appear occasionally, even in the human female, so large as to simulate the nipple itself." Cloquet (1825, p. 518) mentions that the areola shows a number of little eminences, circularly arranged, which become particularly obvious during lactation, and that the majority of anatomists regard them as sebaceous glands, but that Meckel, Morgagni and Winslow all assert that they have seen milk issue from these orifices. A sebaceous content of the areolar glands would be consistent with the function mentioned above of preventing that excoriation which may render suckling almost an agony.

Yet the mammary gland is universally accepted nowadays as a modified sweat gland on account of its microscopic structure, its method of secretion and its development. So, transitional glands would be those between true mammary and true sweat glands, and if the areolar

glands are of this character one would expect them to be, as Maclise suggests, sudoriferous in character and not sebaceous and thus unable to exert any emollient effect on the skin.

Any account of the anatomy of the breast would probably be considered incomplete without some reference to its lymphatic drainage. While it has been my object not merely to repeat those facts about the breast which can be found in the standard textbooks, I would call attention to a recent paper by Sir Cecil Wakeley (1948) in which he gives it as his opinion, which, he says, may not be shared by others, that there is no connexion of the lymphatics of the breast with the supraclavicular glands except through the intercostal spaces and thence via the internal mammary lymph glands.

Such an anatomical account as I have given may have taken away the romance from the Female Breast; may I therefore conclude with a quotation from an entertaining book by Snoop (1928) entitled "From the Monotremes to the Madonna": "The breast is the last word in anatomical motherhood. It is the pinnacle of maternity. In evolution experiments with regard to position were attempted, with regard to number, with regard to size, until finally, with the emergence of Eve and her pair of pectoral breasts, the morning stars sang together and all the sons of God shouted for joy."

## REFERENCES


BRESSLAU, E. (1920) *The Mammary Apparatus of the Mammalia.* London: Methuen & Co.

CLOQUET, J. (1825) *Manuel d'Anatomie Descriptive du Corps Humain.* Paris: Béchet Jeune.

COOPER, ASTLEY P. (1840) *On the Anatomy of the Breast.* London: Longman, Orme, Green, Brown and Longmans.

FRAZER, J. E. (1931) *A Manual of Embryology.* London: Baillière, Tindall and Cox.

HICKEN, N. F. (1937) Radiographic demonstration of breast lesions. *Radiogr. & Clin. Photogr.* **13**, 2-9.

MACLISE, J. (1856) *Surgical Anatomy.* 2nd ed. London: John Churchill.

MONTGOMERY, W. F. (1837) *An Exposition of the Signs and Symptoms of Pregnancy, the Period of Human Gestation and the Signs of Delivery.* London: Sherwood, Gilbert & Piper.

PATTEN, B. M. (1947) *Human Embryology.* London: J. & A. Churchill, Ltd.

SNOOP, F. Z. (1928) *From the Monotremes to the Madonna.* London: John Bale Son & Danielsson.

TODD, R. B. (1847) *The Cyclopædia of Anatomy and Physiology*, 3. London: Sherwood, Gilbert & Piper.

WAKELEY, CECIL (1948) Carcinoma of the breast and its treatment. *Brit. Med. J.* **2**, 631-635.

# "OBSERVABLES" AT THE ROYAL COLLEGE OF SURGEONS

## 17. RECORDS OF ADMIRAL HORATIO NELSON'S WOUNDS

FOR MANY YEARS there was close association between the fighting Services and the Royal College of Surgeons, and the Corporations which preceded it. Under the Charter of 1629 granted by Charles I to the Barber-Surgeons' Company a Court of Examiners was appointed and was entrusted with the duty of examining and approving candidates for the post of Surgeon or Surgeon's Mate for ships in the Navy or Mercantile Marine. Under varying conditions these duties continued to be carried out until early in the nineteenth century.

When a candidate was approved "the qualification was delivered to the party sealed up to be carried to the Navy Office." No fee was charged, but the Master commonly intimated to the Sea-Surgeon what contribution he was expected to give to the poor box. "If he was not in a capacity it was not insisted on."

In 1739, Tobias Smollett was approved for the post of Second Mate on a third-rate ship, and in *Roderick Random* he describes the procedure and mentions fees of five shillings for the poor box, three shillings and sixpence for the beadle, and one shilling for the woman who cleaned the hall.

In 1745, after separation from the Barbers' Company, the new Company of Surgeons was entrusted with the duty of examining candidates for the Army Medical Service as well as those for the Navy. The East India Company also sent their candidates for examination.

The Charter of 1800 (40, George III) creating "The Royal College of Surgeons in London" required the Court of Examiners, upon Request of the Commander-in-Chief or the Lord High Admiral or other authorised Officer of the Crown: "to examine every Person who shall be a Candidate to be approved to serve as a Surgeon or Assistant Surgeon in any Regiment, Troop, Company, Hospital or Garrison of Soldiers . . . or to serve as a Surgeon or Surgeon's Mate appointed on Board any Ship or Ships . . . and shall also in like manner examine all Surgeons' Instruments to be used in our Service which they shall be required in like manner to examine, and shall return such Instruments when examined to such Person or Persons as shall be appointed to receive the same . . ."

As time went on the Examiners were invited to perform functions other than testing the candidates' professional knowledge. In 1764 we find in the minute book the report of a compensation case, and after this date similar compensation and superannuation cases were recorded frequently. Among the records are many of great historical interest. Two of them dealing with Nelson's injuries are reproduced in facsimile on the opposite page.

W-J.

At a Private Court of Examiners holden at their House in Lincolns Inn Fields the 12th day of October 1797.

George Sewell - - - - - Surgeon to an African Ship

Rear Adm.l Sir Horatio Nelson K.B. - applied for Examination in consequence of a Wound received in his Eye & the Court was of opinion that the Injury received by him is fully equal to the loss of an Eye. -

At a Court of Examiners holden at their House in Lincolns Inn Fields the 1st day of March 1798.

Admiral Sr Horatio Nelson - Claimed £135..1..0 for the Chirurgical and Medical Expences of the Cure of his Arm which was thought reasonable & allowed. -

Records of Admiral Horatio Nelson's Wounds.

# OPENING OF RESIDENTIAL QUARTERS

## Royal College of Surgeons of England

---

ON MONDAY, MAY 2, graduate students took up residence in the College for the first time. They are being accommodated in two houses adjoining the College buildings, and this beginning may be regarded as the first stage of the larger scheme of which the "Nuffield College of Surgical Sciences" will be the ultimate development.

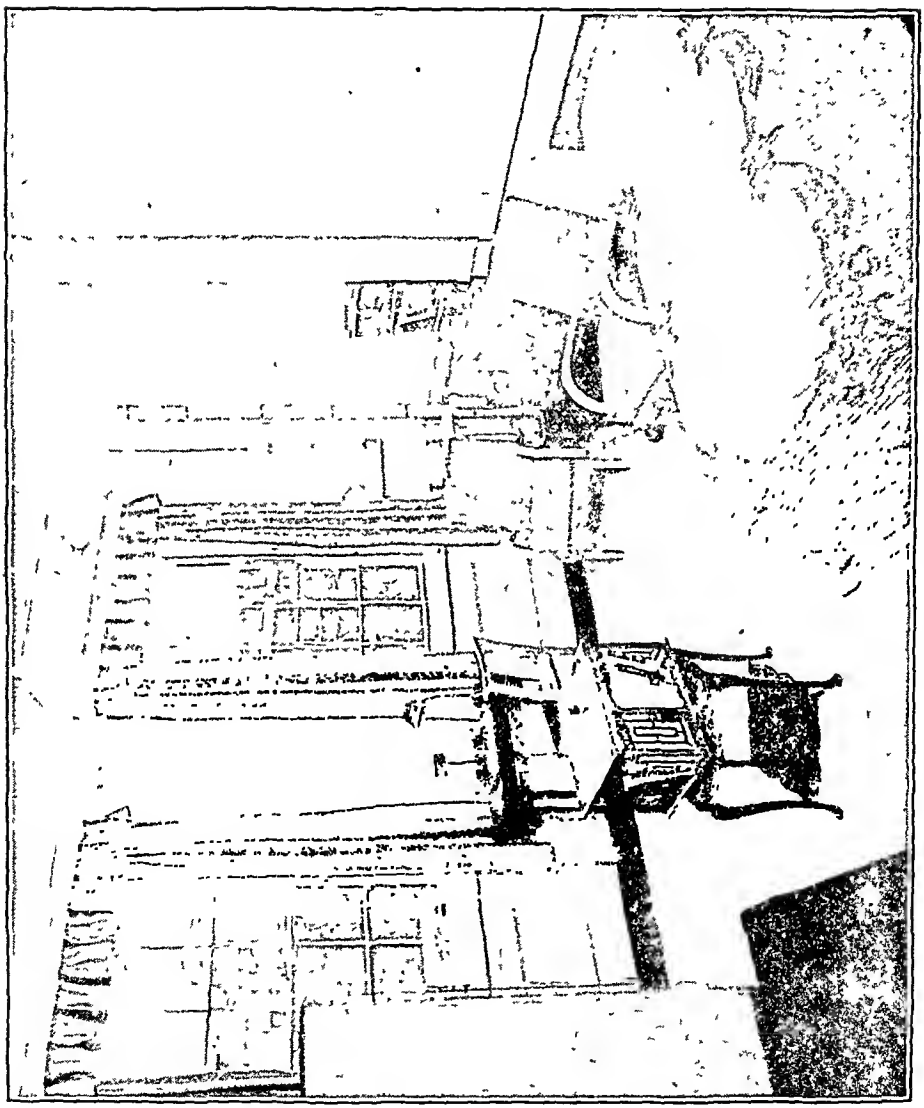
As is well known, the Council have for some time been following a policy of providing facilities and amenities for young surgeons, particularly those from the Commonwealth, the United States and other countries, who come to Britain for advanced study. The need for residential accommodation was obvious if graduates were to be able to make the fullest use of the museums, library and laboratories of the College, and at the same time gain the advantages of Collegiate life.

As so often happens in adapting existing houses for a different purpose from that for which they were designed, many difficulties and problems were encountered. The two houses concerned are Nos. 44 and 45, Lincoln's Inn Fields and communication has been established between the two at ground, second and third floor levels. There is accommodation for over twenty residents with two Common Rooms and a study room. On the ground floor is the Postgraduate Education Office, and across the garden is a Warden's House. The first Warden is Mr. R. J. Last, Lecturer in Anatomy.

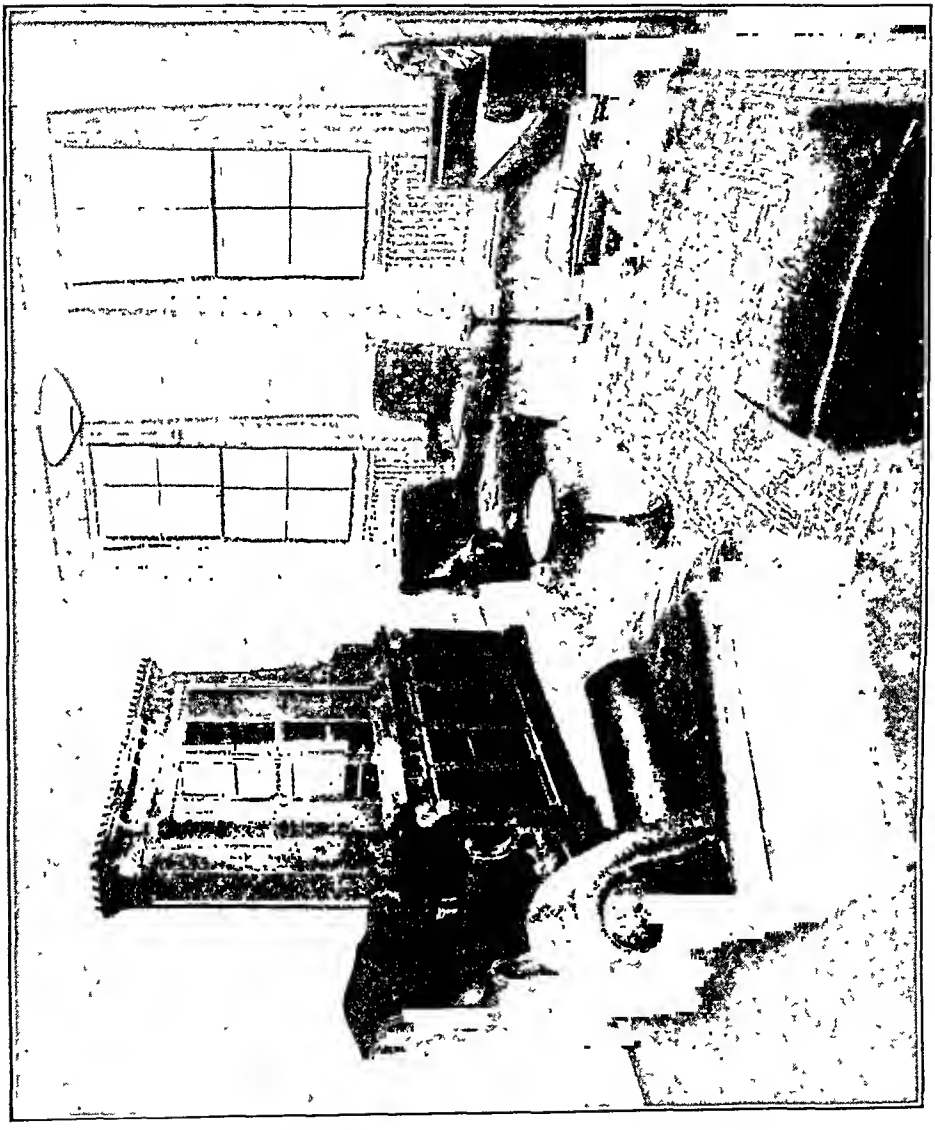
Architecturally the houses are very interesting. Number 44 was built originally in 1638 and records indicate that it was rebuilt in 1700. The house has a beautiful oak staircase. The staircase hall is panelled and has a carved cornice surrounding a painted ceiling representing female figures and amorini against a background of sky. This painting is either by Thornhill, Hogarth's father-in-law, or by one of his pupils.

The original house on the site of Number 45 was erected in 1639, and the present house was built about the middle of the 18th century.

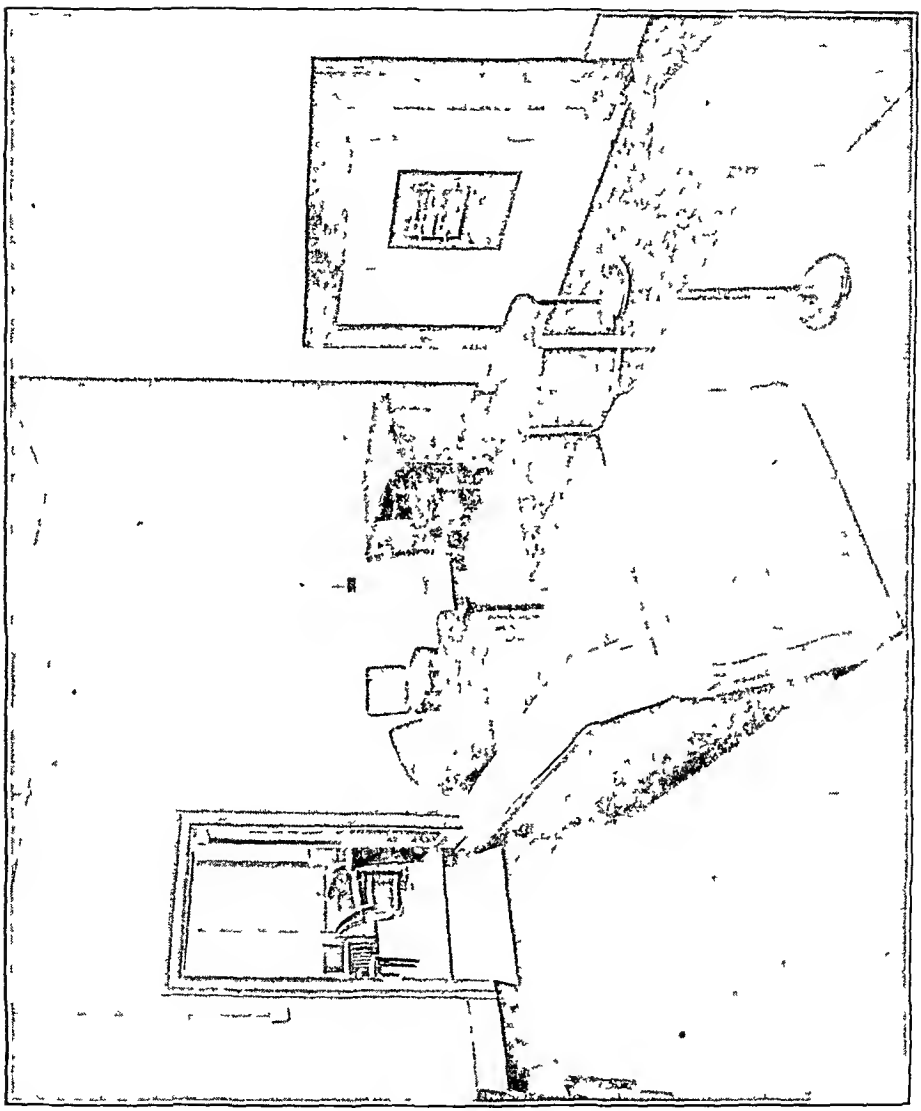
Among the first favoured few who have been given rooms there are students from Australasia, Canada, South Africa, the United States, China, India, Ireland and English Provincial centres. It is hoped that those who have the privilege of living in the College will be imbued with something of the spirit of the Collegiate life of our older residential universities, and that they will meet the leading teachers of Great Britain and distinguished visitors from other countries. Thus they will make contacts which will be valued memories throughout their lives.



A BED-SITTING ROOM



STUDY ROOM



COMMON ROOMS

# THE LIBRARY

## EDWARD JENNER, born 17 May 1749

### On the Cow Pox, the original paper

---

EDWARD JENNER was born 200 years ago on 17 May 1749. He was in his 50th year when he published his account of the cow-pox or "vaccine disease," and advocated preventive inoculation for small-pox with this mild virus, instead of the dangerous virus of small-pox itself, which had been the accepted practice for more than half a century. Jenner was a country practitioner, trained in London at St. George's Hospital, the favourite pupil of John Hunter. He took no degree by examination and was never elected into membership of any of the London medical corporations, though he belonged to the Medical Society of London and the Royal Medico-chirurgical Society. His M.D. was from St. Andrew's University, by nomination.

Country life was still feudal in its social stratification, and Jenner, who was related by birth and marriage to the leading families of north Gloucestershire, had the chief practice there, riding his white horse from manor-house to manor-house. He was much more than an excellent general practitioner. His scientific ability was recognized by John Hunter and Joseph Banks, the best biologists in the country. They encouraged him in the study of natural history, and had secured his election as a Fellow of the Royal Society. His published papers on the cuckoo and on bird migration are based on careful anatomical and physiological investigations as well as prolonged observation in the field. He had also helped Hunter materially, in his work on hibernation especially. Hunter died in 1793, but Jenner retained the friendship of several leading London surgeons of his own standing; he was a close friend of Matthew Baillie and the intimate consultant of Caleb Hillier Parry of Bath, the two most penetrating physicians of the time.

Jenner's interest in the possibility of inoculating against small-pox with one or other milder animal pox was well known for at least ten years before his book was published in June 1798. He had experimented with horse-pox and swine-pox before making his decisive cow-pox inoculation in May 1796. When he had satisfied himself that cow-pox was a safe preventive of small-pox, he wrote in 1797 an account of his experience which he sent to Everard Home, Hunter's brother-in-law, in the hope that it might be submitted to the Royal Society. It was read by Home, Banks and others, but never formally submitted. This original paper, entirely in Jenner's own handwriting, is a most distinguished treasure

13 Case XX.th

The more accurately to observe the progress of the infection, I selected a healthy Boy about eight years old for the purpose of inoculation for the Cow-pox. The matter was taken from a suppurated sore on the hand of a Dairy Maid, Who was infected by her Master's Cows, and it was inserted, on the 14th of May 1796, into the Arm of the Boy, by means of two superficial incisions, each about three quarters of an inch long. On the 7th day he complained of uneasiness in the axilla & on the 9th he became a little chilly, lost his appetite and had a slight head ach. During the whole of this day he was perceptibly indispos'd, & had rather a restless night; but, on the day following, he was perfectly well. The appearance, and progress of the incisions to a state of maturation, were pretty much the same as when produced in a similar manner by variolous matter. The only difference which I perceived, was, that the edges assumed rather a darker hue, and that the efflorescence spreading round the incisions, took on rather more an erysipelatous look, than we commonly perceive when variolous matter has been made use of for the same purpose.

Title Point

VACCINATION : THE FIRST CASE
Edward Jenner's autograph history

On the 1st of July following this Boy was inoculated with the Matter immediately taken from a small pox Pustule. Several Punctures and slight incisions were made in both his arms, and the matter was well rubbed into them, but no disease followed. The same appearances only were observable on the arms, as when a Patient has had variolous matter applied, after having either the Cow-pox, or the small Pox*. (May 14 blue book)

* During the whole time these Experiments were going forward, the Boy slept in a bed with two Children who never had been affected with either of these diseases, but neither of the Children became indisposed in consequence ///

in the College Library. Jenner himself has written on the wrapper: "On the Cow Pox—The original paper"; the heading of the text is simply: "An Inquiry into the natural history of a disease known in Glostershire as the Cow-pox." Jenner's own written description of the crucial case is now reproduced for the first time. This manuscript was among the papers acquired from the Jenner family by Sir James Paget, President in 1875, and presented by him to the College.

Jenner's announcement of vaccination was probably the greatest single contribution to the health of humanity, both for its own value and because the whole science of immunity has developed from it, as Pasteur himself pointed out. Jenner's evidence was by modern standards insufficient, but he was sure that he was right and was fired with a fervent missionary zeal, which made him intolerant of criticism and jealous fo possible rivals. In private life he was by every account a most delightful and stimulating companion. His natural simplicity and goodness of heart were quite unaffected by his world-wide fame, for vaccination swept round the world in the decade following 1798.

## MONTHLY DINNERS

Monthly dinners are held in the College on the second Wednesday of each month. The following are entitled to attend with their guests: All Diplomates and students of the College, and Members of the Associations linked to the College through the Joint Secretariat. It is not necessarily intended that guests should be members of the medical profession.

The dinners will be at 7 p.m. on the following Wednesdays: June 8, and July 13, 1949. There is an inclusive charge of £1 5s. (including drinks), which must be sent with the application to the Assistant Secretary at least a week before the date of the dinner. The dress is Lounge Suit or Uniform.

---

## DIARY FOR MAY (16th - 31st)

| | | |
|---|---|---|
| Mon. 16 | | Final Fellowship Oral Examination (General Surgery) begins. |
| | 3.45 | DR. F. A. FELL—Anatomy of Pronation and Supination of the Forearm. |
| | 5.00 | PROF. A. HEMINGWAY—The Control of Breathing. |
| Tues. 17 | 4.00 | SIR EDWARD MELLANBY—Jenner Oration—Jenner and His Impact on Medical Science.* |
| | 5.30 | PROF. A. HEMINGWAY—Physiology of Exercise. |
| Wed. 18 | 3.45 | DR. E. L. PATTERSON—Orbital Contents. |
| | 5.00 | DR. J. E. CATES—Renal Function. |
| Thur. 19 | 3.45 | PROF. D. V. DAVIES—Cerebral Circulation. |
| | 5.00 | DR. J. E. CATES—Renal Function. |
| Fri. 20 | | Voting Papers for Faculty of Dental Surgery Board Election issued. |
| | 4.00 | PROF. THOMAS NICOL—The Kidneys, Ureters and Bladder. |
| Mon. 23 | 3.45 | PROF. F. WOOD JONES—The Muscles of the Body Wall. |
| | 5.00 | DR. A. C. CROOKE—Adrenal Hormones. |
| Tues. 24 | 3.45 | PROF. F. GOLDBY—The Facial Nerve. |
| | 5.00 | DR. W. FELDBERG—The Autonomic Nervous System. |
| Wed. 25 | 5.00 | SIR GORDON GORDON-TAYLOR—Harveian Lecture—The War Collection.* |
| Thur. 26 | 3.45 | PROF. T. B. JOHNSTON—The Tympanic Cavity. |
| | 5.00 | DR. W. FELDBERG—The Theory of Chemical Transmission of Nerve Effects. |
| Fri. 27 | 3.45 | PROF. T. B. JOHNSTON—The Anatomy of the Cerebrospinal Fluid. |
| | 5.00 | DR. C. C. N. VASS—Digestion. |
| Mon. 30 | 3.45 | DR. C. HOWARD TONGE—Lymphatic Drainage of the Head and Neck. |
| | 5.00 | DR. C. C. N. VASS—Digestion. |
| Tues. 31 | 3.45 | PROF. JOHN KIRK—Autonomic Innervation of the Head and Neck. |
| | 5.00 | PROF. A. C. FRAZER—Fat Absorption and Metabolism. |

*Not part of courses.

# DIARY FOR JUNE

| | | | |
|---|---|---|---|
| Wed. | 1 | 3.45 | PROF. F. G. YOUNG—Endocrines and Carbohydrate Metabolism. |
| | | 5.00 | DR. A. A. MILES—Antigen Analysis. |
| Thur. | 2 | 3.45 | PROF. F. G. YOUNG—Endocrines and Carbohydrate Metabolism. |
| | | 5.00 | DR. A. A. MILES—Bacterial Hypersensitivity. |
| Sat. | 4 | | College closed. |
| Tues. | 7 | | College re-opens. |
| Wed. | 8 | 3.45 | PROF. J. D. BOYD—The Development of Cardiovascular and Alimentary Systems. |
| | | 5.00 | SIR CECIL WAKELEY—The Blood Supply of the Mid-Gut. |
| | | 7.00 | Monthly Dinner for Fellows, Members and Licentiates (see page 335). |
| Thur. | 9 | | Annual Election of Examiners. |
| | | | Pre-Medical Examination and D.P.M. Examination (Part I) begin. |
| | | 5.00 | PROF. GEOFFREY JEFFERSON—Lister Oration.* |
| Fri. | 10 | | Final L.D.S. Examination (Part I) and D.L.O. Examination (Part I) begin. |
| Mon. | 13 | 3.45 | PROF. J. Z. YOUNG—Nerve Repair. |
| | | 5.00 | DR. C. A. KEELE—Chemotherapy I. |
| Tues. | 14 | 3.45 | PROF. J. Z. YOUNG—Nerve Repair. |
| | | 5.00 | DR. C. A. KEELE—Chemotherapy II. |
| Wed. | 15 | 3.45 | PROF. H. A. MAGNUS—Gastric Cancer. |
| | | 5.00 | DR. D. J. BELL—Carbohydrate Metabolism. |
| Thur. | 16 | | First Membership Examination, Final L.D.S. Examination (Part II), and D.P.M. Examination (Part II) begin. |
| | | 3.45 | DR. D. J. BELL—Carbohydrate Metabolism. |
| | | 5.00 | PROF. WILSON SMITH—The Host-Parasite Relationship in Bacterial Infections : (i) Invasion Factors. |
| Fri. | 17 | | D.L.O. Examination (Part II) begins. |
| | | 3.45 | DR. H. L. MARRIOTT—Water and Electrolyte Balance. |
| | | 5.00 | PROF. WILSON SMITH—The Host-Parasite Relationship in Bacterial Infections : (ii) Defence Reactions. |
| Mon. | 20 | 3.45 | DR. H. L. MARRIOTT—Water and Electrolyte Balance. |
| | | 5.00 | PROF. LORD STAMP—Principles of Immunity in Relation to Surgical Practice. |
| Tues. | 21 | 3.45 | LT.-COL. W. H. HARGREAVES—Antibiotics. |
| | | 5.00 | PROF. LORD STAMP—Some Practical Applications of Bacteriology to Surgery. |
| Wed. | 22 | 3.45 | DR. MICHAEL KREMER—Visceral Sensation. |
| | | 5.00 | MR. SOL.M. COHEN—Traumatic Arterial Spasm. |
| Thur. | 23 | 4.00 | PROF. A. KEKWICK—Nutrition and the Surgeon. |
| | | 5.15 | MR. R. W. REID—Disordered Renal Function : the Surgeon's Point of View. |
| Fri. | 24 | | L.D.S. Examination (General and Special Anatomy and Physiology) and D.P.H. Examination (Preliminary) begin. |
| | | 3.45 | PROF. A. KEKWICK—Nutrition and the Surgeon. |
| | | 5.00 | MR. R. W. REID—Disordered Renal Function : the Surgeon's Point of View. |
| Tues. | 28 | | Final Membership Examination begins. |
| Wed. | 29 | 5.00 | PROF. SIR HORACE EVANS—Hunterian Lecture—Hypertension.* |
| Thur. | 30 | | D.P.H. Examination (Final) begins. |
| | | 5.00 | PROF. ARNOLD SORSBY—Streptomycin in Ophthalmology.* |

*Not part of courses.

# JOHN HUNTER AND HIS MUSEUM

An Address delivered to the Osler Club

on

10th December, 1948

by

Professor F. Wood Jones, D.Sc., F.R.S., F.R.C.S.
Sir William Collins Professor of Human and Comparative Anatomy,
Royal College of Surgeons of England

SO MUCH HAS been written concerning John Hunter that it would be foolish to imagine that anything new could be added to the biographical details accumulated in the numerous Lives that have been published during the century and a half since his death. One reason only may be urged in justification of my undertaking to address the Osler Club upon the subject of the Hunterian Museum. It is, I believe, impossible to appreciate the meaning of his great collection of specimens unless we have some understanding of the mentality of the man who lavished so much of his time and his fortune on its preparation. Perhaps it is unfortunate that almost without exception those who have written about John Hunter have agreed in terming him a genius. But, although I defer to no one in my admiration of John Hunter, I do not believe that the term "genius" may be applied with any propriety to his peculiar turn of mind. It is not until we have freed ourselves from the idea that Hunter was a genius that we may form a just opinion of the meaning of his Museum. It is, therefore, worth while to probe once again into Hunter's life and works to enquire if in them we may find some clue to the type of mind and to the manner of thinking possessed by the founder of our Museum.

I can find no short cut in attempting to define what I believe to be the keynote to the understanding of Hunter's cast of mind. It is, therefore, by a somewhat roundabout way that our approach is made and this is so for the reason that it is often the apparently trivial circumstances that influence and ultimately determine the mental outlook of the individual. In Hunter's case, I believe it was the chance that, possessing the intelligence of the ordinary Scots country lad, he escaped the levelling routine of formal education, and so carried into adult life the inquisitive, curious and restless mentality of the days of his apparently idle, but in reality intensely occupied and observant boyhood.

All of us, since we are human beings, are heirs to knowledge concerning one form of life. As human beings we may understand, without teaching and without much quest for knowledge, certain things about other human beings. We know the needs, the desires, the emotions and the reactions of others, since we share these things in some degree with all humanity. Some of us, being members of the medical profession, may flatter ourselves

that we know rather more than that, since we are instructed as to the mysterious processes that are carried out in the hidden places of the human body and even in the human mind. 'Homo sum, nihil humani a me alienum puto' is the motto of the institution wherein I served my apprenticeship to medicine.

So vast is the accumulated knowledge concerning life, as life is lived by mankind, that we may well think that, when we have acquired a sufficient familiarity with it, our cup of learning is full. But it must be admitted that life as lived by mankind is only a very minor aspect of life itself when life is regarded as a whole. The dictum that the proper study of mankind is man may perhaps be accepted somewhat too literally. It is indeed a proper study, but human life must be ranked as no more than a more or less familiar part of the long track that leads from the mysterious coming of life to its equally mysterious going in all things in which this quality of life is manifest.

We may justly claim to an innate knowledge of many of the factors of human life. We may put ourselves in the place of our fellows and realise the purposes that dictate their actions. We may understand their feelings and emotions and appreciate the motives for their overt conduct. May we go much further afield in the realm of life than that? Is it permitted to us that we may form a just conception of the factors of life in other animals? Even if we cannot answer the question "How?", might we aspire to answering the question "Why?" when considering the behaviour of other living things?

I think it is true to say that the more highly educated members of mankind who dwell in the cities of civilization are almost prohibited from making any real steps, in advance of their knowledge of themselves and of their fellows, towards an understanding of the lives of lesser things. If fault may be found with certain researches into animal psychology it might be said that the highly educated and civilized observer of animal behaviour must needs manifest an unusual aptitude for detachment if he succeeds wholly in escaping from the temptation of interpreting the reactions of other forms of life in terms of his own psychological experiences. And yet I am sure that anyone who has had intimate commerce with those human races still living primitive lives and having no written language, must have realised that their understanding of the essentials of life extended to all the living things important or familiar in their immediate environment. An Australian native has an intense realisation of the overt manifestations of life in all those living things with which he is familiar in his daily round. He knows their manner of life. He realises the mainsprings of their actions. The "Why?" of their behaviour is patent to him, even if he does not concern himself with the "How?" of it. He does not read his own psychological composition into the behaviour of a 'goanna, but he takes the psychological composition of the 'goanna unto himself and acts, in order to effect its capture, on the basis

of 'goanna psychology and not upon the basis of his own. It is no very easy matter to make this fundamental truth real, or even apparent, to men whose lives have always been spent in the habitations of man and who have, in consequence, ceased to rub shoulders on terms of familiarity with the other living products of nature. Yet it is true that, even in our Western civilization, there are still some men, near to the soil and almost untouched by education, who possess this ancient knowledge. The real countryman still exists in rural Britain—the man who, if he wishes to capture some wild creature, can still call upon this primitive aptitude of *knowing* what life and its reactions are in living animals other than human beings. And let us confess at the outset that it is commonly the countryman who has been least subjected to academic education who retains his ancient heritage of knowledge. It would seem possible that the highway of academic learning may lead the seeker after knowledge of life away from those by-paths in the travelling of which real knowledge of life and living may be encountered.

It was the Richard Jefferies who, as a country boy, wandered solitary in the fields around Coate Farm that wrote those studies of the life of the hedgerows for which he is justly famous. It was the Richard Jefferies who was the attentive pupil at Swindon School and later was a newspaper man on the staff of the *North Wilts Herald*, that wrote the ludicrously unreal novels by which he fancied fame would come. Jefferies *knew* of the life and the urges of the living things of the countryside; they were part of his own inborn and instinctive knowledge. But when he attempted to translate what he had learned by reading into the terms of real life he failed completely. Between the real knowledge of life that grew from his youthful familiarity with Nature and the concepts gleaned from his academic studies there was always conflict, the conflict he so painfully revealed in "The Story of My Heart."

With John Hunter there was no such conflict. The truant boy who wandered the fields around Long Calderwood and, as he himself tells us, "watched the ants, bees, birds, tadpoles and caddis-worms," became the man who, with his youthful knowledge unforgotten, still watched the bees and still bred tadpoles. For John Hunter there was no break, no divorce from his boyhood knowledge by reason of a newer love for academic learning. He "could not be taught to read but with the greatest difficulty and long after the age when other children read English fluently." "He hated his school books" and as he tells us, "cracked like so many vermin" the plans made for sending him to Oxford to "stuff Latin and Greek." His mind was that of an intelligent boy, interested in the living things of the countryside and curious as to their ways and manner of life. This insatiable curiosity he retained throughout his life and, happily for science, chance gave him the opportunity for satisfying it by the work of his hands. The beasts of the farm and the creatures of the hedgerow had taught him of function and awakened a keen desire for further knowledge. He was fortunate in that his youthful

curiosity, natural to all intelligent children, was not quenched by the routine of formal education. He was 20 years old when he came, uncouth and untutored, to London but at least he retained what so many have lost at half that age—an intense wonder as to the " Why ? " and " How ? " of life and living. He was highly intelligent and understanding ; curious and vastly industrious : but it is much to be doubted if the term " genius " rightly applies to him.

If we have formed any just estimate of Hunter's intellectual pecularities and of his outlook on life, it is perhaps more simple to determine the purpose that underlay his vast expenditure of industry in the formation of his Museum of Natural History specimens. The Hunterian collection of preparations has been described as an Anatomical Museum. By some, who have felt that they were more informed as to his purpose, it has been regarded as a Physiological Museum. By others, who realised that it was something more than either of those, it has been held to be a collection of specimens illustrating his conceptions of life.

Now we may well agree with the opinion of a contemporary (Abernethy) that " he had not the happy talent of displaying the stores of his mind, nor of communicating to others the same perception of the importance of his facts and opinions as he himself entertained." But even making this concession, it must be admitted that Hunter's written expression of his conceptions of life, as such, are so nebulous as to preclude the possibility of any concrete illustration of them by means of a series of specimens. He believed in a Living Principle which " is not simply diffused, but is combined, or makes one of the constituent parts of the whole." This Living Principle had, as its basal expression, a quality he termed " Simple Life " : and Simple Life was manifest in what Owen translated into modern terms as " irritability." Life as a philosophical concept was something that Hunter (even when his text is helped out by Owen's parenthetical notes) was quite incapable of expressing and no intellectual shortcoming may be imputed to him in that regard. Nor was the understanding of Hunter in any way assisted by John Abernethy's lecture on " Mr. Hunter's Theory of Life " published in 1814, for Abernethy, impressed by the work of Sir Humphry Davy and Volta, came to the conclusion that " If the vital principle of Mr. Hunter be not electricity, at least we have reason to believe it is of a similar nature." John Hunter had been dead for 20 years when Abernethy propounded the electrical interpretation of his theory of life in order to make it more acceptable to a newer generation ; but I feel that Hunter would not have welcomed with any great enthusiasm this physical simplification of something of which he was unable to form or to express any concrete conception himself. Most certainly he did not spend laborious days preparing specimens to illustrate a conception of life based upon the phenomenon of electricity. John Hunter knew no more than any of us do what the essential nature of life may be : but he had the keenest appreciation of how life manifests itself in function. He *knew* of the life of trees and insects and the creatures of the countryside

as the intelligent countryman knows of these things: he did not form a coherent philosophical concept as to the nature of life itself and there is small blame to him on that account.

In his notes on an Introduction to Natural History there lies, I believe, the clue to his life activities and to the meaning of his Museum. Writing under the heading " On the Study of Natural History," he says, " Writers on the Natural History of animals have been of two kinds—one (concerned in) only what they could observe externally, such as form and mode of life ; the second (studying only) the internal parts and the structure of the whole animal, which was performed by the anatomist. As the (subject of the) first has an immediate connection with (that of) the second, the describers of form conjectured what the structure ought to be by consulting the work of the anatomist; and the anatomist conjectured what the living history is or ought to be from the Natural History of the others; filling up what he conceived to be just, and fancy supplying the rest. But such union of knowledge does not properly match. It is one building built at different times—an addition to an original plan. It is no wonder, therefore, that the whole is imperfect."

In this not very clearly expressed jotting down of his notes, I believe that Hunter gave voice to the mainspring of his life's work in Natural History. He realised that, if real progress in the knowledge of living things were to be made, a synthesis must be effected; for no advance was possible if one set of workers was confined to the study of function, while lacking first-hand knowledge of structure, and that anatomical studies divorced from a knowledge of function were like to prove sterile. The student of structure must of necessity be instructed in function. The almost untutored country boy from Long Calderwood *knew* of the life of living things as he had seen it in intimacy. He appreciated function—the function he had witnessed in the farmyard and in the hedgerows. He already possessed one great asset. The other fell into his lap when, coming to London at his brother William's invitation, he had at his disposal all the facilities for the study of the structure of the various forms of life. He realised that by his own personal efforts the possible synthesis of function and structure might be achieved. And to that end he devoted his life's labour. John Hunter's Museum is neither an anatomical nor a physiological Museum. It is both; but its wholeness is something far greater than the sum of its two parts. Regarded as an expression of scientific progress, it is the first and still the only attempt to display the interdependence of structure and function in the expression and the maintenance of life as a whole. Regarded in terms of the man John Hunter, it is the product of laborious years spent in the dissection of preparations of animal structure based on the innate knowledge of life and function gleaned by the intelligent but untutored lad who, in the eyes of his seniors, idled away his time roaming the countryside around Long Calderwood.

# SOME OBSERVATIONS ON THE PATHOLOGY AND SURGICAL TREATMENT OF LABYRINTHINE VERTIGO OF NON-INFECTIVE ORIGIN

Hunterian Lecture delivered at the Royal College of Surgeons of England

on

2nd February, 1949

by

Terence Cawthorne, F.R.C.S.

Surgeon for Diseases of the Ear, Nose and Throat, King's College Hospital, Aural Surgeon, National Hospital for Nervous Diseases, Queen Square.

## INTRODUCTION

ALTHOUGH AN ASSOCIATION between vertigo and deafness has been recognised since the days of Hippocrates, it was not until 1861 that Meniere declared that the labyrinth was the seat of the disorder responsible for these and the associated symptoms of tinnitus, nausea and vomiting. In the first century A.D., Soranus noted the following group of symptoms which he attributed to epilepsy or other intracranial disease. " Heaviness and giddiness in the head, an inner noise which is felt in the occiput too, tension in the eyes, ringing in the ears or difficulty in hearing, together with vertigo."

But men of letters as well as doctors have commented on this group of symptoms, one being that wise observer and recorder of human life, Shakespeare. In the First Act of *Julius Cæsar* Shakespeare draws attention to Cæsar's physical defect, which had always been attributed to epilepsy, as follows : Act 1, Scene 2 : Cæsar to Antony : " Come on my right hand for this ear is deaf." And a few lines later, Brutus to Casca (about Cæsar) : " 'Tis very like he hath the falling sickness."

The falling sickness, Temkin (1945) has always been attributed to epilepsy, though many other diseases, including labyrinthine vertigo, have been included under this heading. In the case of Julius Cæsar the combination of unilateral deafness with the falling sickness in an otherwise robust and active man of early middle age must surely refer to a labyrinthine disorder.

A century later, when John Hunter, in whose name this lecture is given, was a young man, Dean Swift, Leslie S. (1928), in a letter to Pope, ended as follows : " This wildness you must allow because I am so giddy and deaf." That Swift suffered from what we know as Meniere's Disease there can be no doubt; though to what extent it contributed to his eccentricity of behaviour is a matter for conjecture. In their efforts to relieve him, Swift's medical advisers lavished their attentions upon his digestive tract, and submitted him to numerous blood-lettings; but Swift stubbornly and as it has turned out, shrewdly maintained that the cause

of his illness lay within his skull, and not in his blood nor yet in his belly. In this connection it is of interest to note that a cast of Swift's brain is in the Hunterian Collection housed in this College. It may be seen in a case at the back of the Lecture Hall.

Interest in the structure, and speculation as to the function, of the labyrinth were in evidence in the early years of the nineteenth century. The general view then held was that the whole of the labyrinth was concerned with the perception of sound, the semicircular canals in particular being responsible for directional hearing. Flourens (1824) was the first to suggest otherwise, when he found that in animals the semicircular canals exerted a modifying influence on body movements. In the winter of 1874-75 three separate observers, Mach (1874), Breuer (1874) and Crum Brown (1875) each, independently of the others, explained the mechanism of the semicircular canals of the vestibular labyrinth in terms which form the basis of our present conception of vestibular physiology; namely, that the end organs of the vestibular nerve in the semicircular canals (cristæ ampullaris) respond to movements of the fluid endolymph inside the canals initiated by acceleratory or deceleratory movements of the head.

Baginsky (1881) noted the effect on balance and eye movement of syringing the ear with cold water; though it was Barany (1906) who explained the significance of caloric stimulation and developed both the caloric and rotatory methods of functional testing of the vestibular labyrinth. For this he was awarded the Nobel Prize in Medicine. The mechanical explanation of these tests has since been confirmed by Steinhausen (1931), who has demonstrated actual movement of the cupula and contained crista ampullaris of the semicircular canals in response to thermal and rotatory stimuli. Breuer (1875) was the first to suggest that the utricle was stimulated by the position of the head in space rather than by rotatory movements, and this has since been confirmed and amplified by Magnus and de Kleyn (1912), Magnus (1924) and McNally (1933).

The labyrinth is also concerned with the perception of sound, which is carried out by the Organ of Corti in the Cochlea.

At first sight it may seem strange that two such diverse functions as hearing and balance are so intimately connected; but the reason becomes apparent when it is appreciated that stimulation of both cochlear and vestibular end organs in the labyrinth is by means of a fluid wave of endolymph, produced in the case of the cochlea end organ by transmitted air-borne sound waves, and in the case of the vestibular end organs by movements of the head.

The frequency with which unnatural vestibular stimulation, such as sea and other forms of motion sickness, or sudden fluctuations in vestibular activity, is followed by nausea and vomiting, pallor, sweating, slowing of the pulse, and other signs of vagal stimulation, suggests an intimate and easily traversed connection between the vestibular and vagal

centres in the brain stem. When the function of the labyrinth is suddenly impaired, even if only for a short while, a very characteristic and dramatic syndrome follows that, since Meniere's original description, quite rightly bears his name ; though it must be said that a more descriptive term would be " Acute Labyrinthine Failure." A less startling picture, the significance of which is not so readily recognisable, is seen when the loss of labyrinthine function is incomplete or is gradual in onset ; and it is found that the degree of severity of the symptoms and signs is in direct proportion to the suddenness and amount of loss of function.

When the lesion that is responsible for this syndrome is confined to the labyrinth, and more often than not this is the case, it never in itself causes death. In consequence the amount of pathological material available for detailed study is very small indeed. Also the preparation of the temporal bone and contained labyrinth for histological examination is difficult and tedious, and there are comparatively few centres where it is practised regularly.

Thus not until 1938 was the true nature of the condition generally known as Meniere's Disease explained by Hallpike and Cairns, as the result of a histological examination of the labyrinths from two cases exhibiting the classical features of the condition. They found that the abnormality lay within the labyrinth, and they considered that the essential mechanism of the disorder was an obstructive distension of the endolymph system. These findings have since been confirmed by other observers, and the term " hydrops of the labyrinth " has been suggested as an additional or alternative description for this disease ; for disease it surely is, and one that can usually be readily recognised.

There are, however, still remaining within the ambit of the term Meniere's Syndrome many conditions, which, though they all include vertigo and many, in addition, deafness, differ widely both in the nature and situation of the lesion. In some a definite cause for the symptoms can be demonstrated in the labyrinth, the eighth nerve, or its central connections ; and the nature of such causes may be post-traumatic, as when the labyrinth is implicated in a basal skull fracture ; inflammatory, as when suppuration extends from the middle to the internal ear; neoplastic, as in acoustic neuro-fibromata ; vascular, as in thrombosis of the anterior inferior cerebellar artery ; toxic, as is seen following extended streptomycin therapy ; or sclerotic, as is sometimes noted in disseminated sclerosis.

In this paper, however, only those cases of vertigo will be considered in which it is thought that the cause lies within the labyrinth and that it is not due to infection.

## PATHOLOGY

The non-suppurative conditions arising within the labyrinth that may give rise to symptoms of labyrinthine failure will be considered under the

heading of Hydrops, Injury, and Hæmorrhage, though, as will emerge, the only two cases of hæmorrhage within the labyrinth that I have actually been able to demonstrate were the result of injury.

Some idea of the relative frequency of these causes may be gained from the following table that tabulates the probable cause in the series of 661 cases of vertigo of non-infective origin that form the basis of this paper.

CAUSES OF NON-SUPPURATIVE LABYRINTHINE VERTIGO

| | |
|---|---|
| Hydrops .. .. .. .. .. .. | 578 |
| Injury .. .. .. .. .. .. | 83 |
| Hæmorrhage .. .. .. .. .. | 2 |
| (Already included under injury.) | |

## HYDROPS

This condition is generally and very appropriately known as Meniere's Disease, for it was Meniere's original paper in 1861 that drew the attention of clinicians to the labyrinth as the seat of the disorder responsible for the syndrome that has since borne his name. This paper, in which he described the case of a young woman who had died after several days of fever, continuous vertigo, unilateral deafness, and vomiting, has been the subject of some criticism, particularly by McKenzie (1924), Dederding (1929) and Atkinson (1941). It seems that Meniere, for some years before the publication of his paper, was convinced, possibly as the result of his translation of Kramer's (1848) textbook on Diseases of the Ear, that the labyrinth was the seat of the disorder responsible for cases of severe vertigo associated with unilateral deafness. In his determination to confirm this theory he took the opportunity presented by this unfortunate girl's death to prove his point. From the course of her illness, which was rapidly fatal, combined with his finding at post mortem of a reddish plastic exudate within the semicircular canals, we are forced to conclude that the condition was due either to infection or hæmorrhage, possibly of leukæmic origin, but certainly not to hydrops. Nevertheless, it seems appropriate that Meniere's name should be perpetuated by association with that large group within the syndrome of acute vestibular failure, namely hydrops.

The possibility that bouts of paroxysmal vertigo associated with deafness, for which no cause could be found, might be due to an increase of endolymphatic pressure was put forward by Knapp and Cheatle over 50 years ago when they compared the condition with glaucoma. Other observers thought along similar lines, and Dederding (1929) drew attention to the part played by fluid balance in the production of the symptoms. Mygind and Dederding (1923) considered that the condition was due to faulty water metabolism, and Furstenberg, Lashmet, and Lathrop (1934) attributed this to the retention of sodium within the body. Wright (1937)

and Crowe (1938) each considered the disease to be due to altered conditions of the endolymph, either as the result of physico-chemical (Crowe) or inflammatory (Wright) changes. Very soon after this Hallpike and Cairns (1938) described the histological changes they found within the labyrinth in two cases of Meniere's Disease, and since then these findings have been confirmed by several other observers, including Hallpike and Wright (1940), Rollin (1940), Lindsay (1942) and Altmann and Fowler (1943). They all found, on the affected side only, an extreme dilatation of the endolymph system; and in some, changes in the absorption area of the endolymph around the saccus endolymphaticus. Nothing to suggest an inflammatory cause for any of these changes was noted. These changes are most apparent in the cochlear part of the membranous labyrinth. The central canal of the cochlear may be enormously dilated and the Organ of Corti compressed.

I have had the opportunity of examining at operation the perilymph space and membranous labyrinth of the lateral semicircular canal with the aid of a binocular dissecting microscope giving ten diameters of magnification, in over 180 patients exhibiting all the features of Meniere's Disease, and although the findings are negative I think that they deserve our attention. In none has there been any deviation from the normal in appearance or rate of flow of the perilymph. The membranous canal and ampulla have in all cases been of normal size and of normal translucency. The standards of normality are based on the appearances at operations for other conditions in which the labyrinth is unaffected, notably Otosclerosis.

The predisposing cause of Meniere's Disease remains unknown. Before its true nature was appreciated, conditions of the middle and even external ear were often blamed; but I have never seen a case without obvious clinical signs of internal ear changes, and the number of instances in which the middle ear plays any part in the causation of the symptoms must be exceedingly small. Wright (1937) believes that a focus of sepsis may be responsible for the attacks comparing the condition with the increased intraocular tension in iritis. Whilst circulating toxins may be responsible for certain cases of vertigo-alcohol and streptomycin may be cited as instances—it is probable that such toxins produce their effect on the vestibular neurones rather than the end organ. Duke (1923), Dohlman (1939), Williams (1944) and others favour an allergic reaction as the exciting cause; but if this were so one would expect to find other manifestations of allergy. In the present series, the number of cases exhibiting any of the usual stigmata of allergy was not larger than might be found in any other group of individuals. Atkinson (1941) considers that either local vasodilatation causing increased capillary permeability or local vasoconstriction resulting in anoxæmia and local tissue œdema may precipitate the attacks. In a later communication in which he reviews the possible causes Atkinson (1946) quotes Ohnell (1932) as the first to

suggest that Vitamin C deficiency, resulting in altered capillary permeability, may be responsible for the attacks.

I think that consideration should also be given to two other possible predisposing factors that I have noted in the history of some of the patients in the present series. In three patients there was a definite history of the attacks starting soon after exposure to blast from high explosive shell or bomb, and though the course of a case of vertigo of traumatic origin is as a rule quite distinct from Meniere's Disease, these three all followed the pattern of Meniere's Disease and all started soon after exposure to blast; still the association may be coincidental. There are, in addition, a number of patients who date their attacks of vertigo from a head injury and who have symptoms that could be mistaken for hydrops, though careful investigation usually reveals a distinction between the two groups. I have another patient who, ever since head injury with labyrinthine involvement, has been subject to bouts of vertigo and nystagmus whenever she puts her head backwards and to the left. This is, of course, a not uncommon sequel of a head injury, but the symptoms are as a rule constant. The interesting feature of this particular case is that there are fairly regular periods of complete freedom from these symptoms, just as is seen in Meniere's Disease, and I cannot help feeling that there may be a link between the two. The actual number of undoubted cases of hydrops that could have been precipitated by a head injury is, however, small, though the association cannot be entirely excluded. In three further typical cases of Meniere's Disease, the attacks started shortly after one labyrinth had been affected by mumps. In both these groups it may be that in some way the preceding injury or disease interfered with the pressure regulating mechanism of the endolymph system.

As regards the exciting cause of the recurrent bouts of hydrops of the labyrinth, for it is these that are responsible for the actual attacks of vertigo, the work of Mygind and Dederding, and Furstenberg (*et al.*) deserves careful study, because, in the presence of an even temporarily closed endolymph system, variations in the fluid content of the body tissues, no matter what the cause, are liable to affect the endolymph pressure. Cawthorne and Fawcett (1938) found that striking variations in the symptoms in cases of Meniere's Disease could be caused by preventing or encouraging fluid retention.

Whatever is responsible for the functional or structural defect that interferes with the pressure regulating mechanism of the endolymph system, the result is that the labyrinth is at the mercy of any condition that favours the retention of fluid within the endolymph system, be it allergy, vasomotor changes, vitamin deficiency, or merely alteration of posture. Successive bouts of over-distension lead to irreversible changes in the end organs of hearing and balance that may finally abolish function and thus end the disease. This may happen quickly in one attack, or

gradually over a period of years, but in my experience complete loss of function and abolition of attacks is not very common.

To sum up, the effects that have been so clearly demonstrated by Hallpike and Cairns, and since confirmed by other workers, are apparently limited to the labyrinth, and are the result of over-distension of an endolymph system that for some unknown reason is unable to adjust itself to variations in pressure to which it may be subjected.

## INJURY

The membranous labyrinth in which are found the delicate end organs of the eighth nerve is carefully protected by being housed within the much larger and very robust bony labyrinth, the intervening spaces being occupied by fluid perilymph in which the membranous labyrinth floats. Despite these precautions the labyrinth may be injured by fractures involving it, or by surgical procedures that may be deliberate or accidental. Furthermore, in virtue of its functions the labyrinth is, in this age of loud sounds and rapid movements, liable to damage by over-stimulation.

The effects of deliberately damaging the membranous labyrinth with the object of destroying function in certain cases of Meniere's Disease, have been noted by Cawthorne, Fitzgerald and Hallpike (1942), Cawthorne and Cooksey (1946), and Cawthorne (1947). It has also been found that a similar, though usually less striking picture, follows when a window is deliberately made in the bony vestibular labyrinth for the relief of deafness due to otosclerosis—the fenestration operation—though here, of course, every care is taken to preserve labyrinthine function. Once the immediate effects of these deliberate operations on the labyrinth have subsided there is left a residuum of symptoms that is very like the remote effects that not infrequently follow concussive head injuries. The striking similarity between these groups, both as regards clinical features and management, led to the suggestion that the site of the injury responsible for the symptoms was identical, Cawthorne and Cooksey (1946). In labyrinthine operations the injury is to the labyrinth and its contained end organs of hearing and balance, but there is not as yet any pathological evidence available to show where the damage is in cases of closed head injury. Nevertheless, the close clinical and therapeutic relationships between the two groups favours a common site of injury.

The possibility of labyrinthine damage being associated with head injuries has been noted by many observers, including S. H. Mygind (1918), Brunner (1928, 1940), Barre and Greiner (1932), Linthicum and Rand (1931), Voss (1934), Glaser (1937) and Barmoel and Marks (1941). The frequency of vertigo as a sequela of concussive head injuries and the possibility of a labyrinthine disturbance in such cases had also been appreciated by Osnato and Giliberti (1927), Russell (1932), Symonds (1937, 1943) and Denny Brown (1943).

At this stage it will be appropriate to consider what may actually happen within the labyrinth when it is subjected to various forms of injury; though it must be said that, as in other disturbances, such injuries are of themselves rarely fatal, so that there is little opportunity for detailed histological examination.

(*a*) *Fractures.* Basal skull fractures may involve the petrous portion of the temporal bone and in doing so will tend to follow the lines of least resistance along the thinner areas of bone, one of which leads right across the thin tegmen tympani. This roofs over the tympanic cavity and sometimes the fracture may extend downwards to reach the labyrinth. In four cases that came to operation a fracture was seen extending into the bony external semicircular canal. In two of these details were obscured by superadded infection; but in the other two, using the binocular dissecting microscope (×10), the perilymph space was seen to be filled with a dark blue jelly-like clot which was considered to be the result of

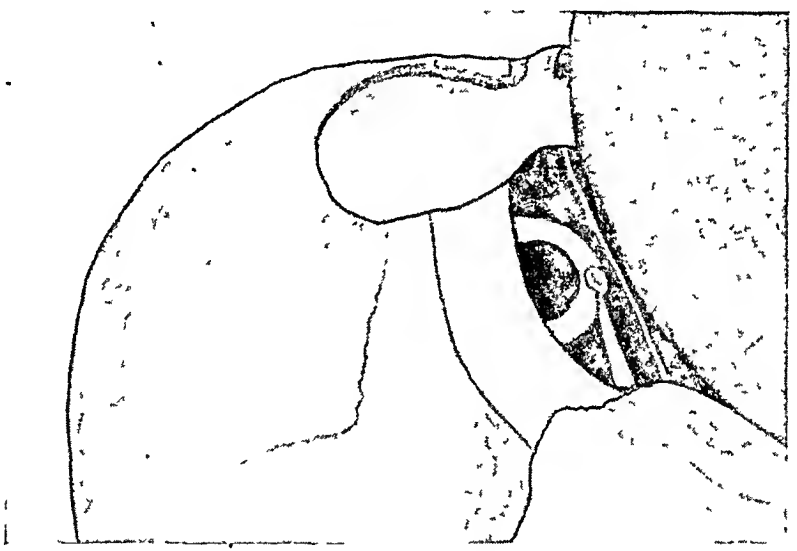


Fig. 1. *Fracture into bony external semicircular canal.* Appearance of fractured canal as seen through binocular dissecting microscope (×10). The incus has been removed, exposing the bony external canal, the facial nerve, the stapes and stapedius tendon, the chorda tympani nerve, and the head of the malleus.

former hæmorrhage. After removal of the clot the membranous canal was found to be intact, though in each case it was altered in appearance and consistency, being pink tinged and roughened, and in one case, collapsed. These are the only cases of labyrinthine vertigo in which I have actually seen evidence of bleeding within the bony labyrinth.

(*b*) *Labyrinthectomy.* In this procedure Cawthorne (1943), which will be described in further detail under "Treatment", the membranous

external semicircular canal is seized and removed, together as a rule with the ampulla. There is no hæmorrhage to be seen at the time of operation but the possibility of hæmorrhage occurring beyond the field of vision at the time or afterwards cannot be excluded. Subsequent infection may also occur, though I have only seen clinical evidence of this in two cases. In cases of Meniere's Disease, for which this procedure is carried out, the result is always total loss of labyrinthine function, both cochlear and vestibular, and I attribute this to the direct result of the injury to the membranous labyrinth caused by removal of its lateral canal.

(*c*) *Other Forms of Labyrinth Destruction.* The membranous labyrinth can be destroyed by injection into the perilymph space of absolute alcohol, Mollison (1931), or the coagulation of the membranous canal by diathermy current, Putnam (1938), Day (1943).

I have employed both of these agents for the relief of vertigo due to Meniere's Disease, and have observed under the dissecting microscope an immediate alteration in the appearance of the membranous labyrinth. In every case so treated by me all labyrinthine function was subsequently lost.

(*d*) *Labyrinthotomy.* The term labyrinthotomy is used when an opening is made in the bony labyrinth. Such a procedure is now frequently employed for the relief of deafness due to otosclerosis and is known as fenestration, Lempert (1938). The opening is made in the dilated anterior end (ampulla) of the bony external semicircular canal, care being exercised not to injure the membranous labyrinth. Every precaution is taken to prevent blood entering the perilymph space, and the opening in the bony canal and ampulla is sealed off by a thin tympano-meatal flap, which adheres to the edges of the window and is maintained there by temporary pressure. Cochlear function is as a rule unimpaired, but the subsequent and often long-standing symptoms of disturbed vestibular function are, I believe, due to altered physical conditions within the labyrinth rather than to hæmorrhage or infection.

This procedure can be compared with the experiments of Ewald (1892), who made openings in the semicircular canals of pigeons without damaging the membranous labyrinth; and from which he made certain observations and propounded certain laws, now considered not to apply to the intact human labyrinth, Cawthorne, Fitzgerald and Hallpike (1942).

(*e*) *Remote Interference with Labyrinthine Function.* Section of the whole of the eighth nerve produces the same effect as destructive operations on the labyrinth ; without, however, causing any histological changes within the labyrinth, over and above those resulting from the causal disease, as Hallpike and Cairns (1938) have shown.

(*f*) *Closed Head Injuries.* It has been found that head injuries may be followed by changes, both in the vestibular end organ in the labyrinth and in its connections in the central nervous system. Brunner (1928), (1940),

showed that blows on the fixed head caused changes within the labyrinth and also others, mainly vascular, in the brain stem and elsewhere in the central nervous system.

Denny Brown and Russell (1941) in an experimental study found that in animals the clinical features of concussion could be produced more easily by blows upon the occipito-parietal region of animals whose heads were free to move with the impact of the blow than when the head was fixed. They termed this "acceleration concussion," and, so far as the signs within the central nervous system were concerned, these were reversible.

Most of the cases of concussive head injury that I have observed with prolonged vertigo have been the result of "acceleration concussion"; and in nearly all there have been demonstrable and, for the most part, irreversible changes referable to the vestibular apparatus.

The following Table shows the result of the vestibular examination in a series of 83 cases of concussion in which vertigo was a prominent sequel:—

POST-CONCUSSIONAL VERTIGO

| | |
|---|---|
| Abnormal Caloric Responses .. .. .. | 79 |
| Normal Caloric Responses .. .. .. | 4 |

Both the cochlear and vestibular end organs have for their appropriate stimulus the displacement or deformation of the end organ by a movement of endolymph. If one end organ sustains damage as the result of excessive endolymph movement it is reasonable to suppose the same may happen with the other.

In the case of the cochlear end organ it has been shown that exposure to very loud sounds may cause visible damage to the Organ of Corti, Lurie (1944).

As for the vestibular end organs, the slightest turning or shift of the head causes movement and deformation of the maculæ of the utricle and the cristæ of the semicircular canals. Should the movement of the head be excessive, as it must be in the type of concussion under consideration, then it seems likely that the part of the nervous system that will be subjected to the greatest strain will be that which is most sensitive to sudden movement, namely, the vestibular end organs. That disordered vestibular function is so frequently found in the post-concussive syndrome is, I consider, strongly in favour of an injury to the labyrinth, Cawthorne and Cooksey (1946). It now remains to produce histological evidence in support of this hypothesis, and once again we are faced with the fact that the cases in which the injury is limited to the labyrinth almost always pursue a benign course, so that pathological material is not available, and I would urge the importance of ensuring that the labyrinth is examined in any fatal case.

## HÆMORRHAGE

Despite the constant and repeated references to hæmorrhage as a cause of labyrinthine vertigo, I have only found actual evidence of intra-labyrinthine hæmorrhage in two cases, each of which was the result of injury. I have not as yet seen a proven case of spontaneous hæmorrhage within the labyrinth. That such a hæmorrhage may take place, particularly in one of the blood dyscrasias is of course possible, but it cannot be common. Occlusion of the artery supplying the labyrinth is known to occur in the anterior inferior cerebellar artery syndrome, but again this is not common and does not really come within the terms of reference of this paper.

## SURGICAL TREATMENT

As far as I can ascertain the first operations upon the labyrinth for the relief of vertigo of non-infective origin were carried out in this country by Lake (1904, 1911), and Milligan (1912), both of whom opened widely the bony semicircular canals. Jenkins (1911) opened thè lateral semicircular canal only, and it is interesting to note that it was for this operation that the term fenestration was first used. Crockett (1914) removed the stapes, and Portmann (1927) drained the saccus endolymphaticus with the object of relieving pressure within the labyrinth. Hautant (1934) punctured the membranous external semicircular canal, and Mollison (1931) injected alcohol into the perilymph space *via* an opening in the bony external semicircular canal. Wright (1938) also injected alcohol into the labyrnth *via* the tympanic membrane and footplate of the stapes, whilst Berggren (1939) used an opening in the promontory. Lempert (1948) has recently described a new technique whereby the labyrinth is drained by removing the stapes and at the same time enlarging the round window. Putnam (1938) and Day (1943) applied a diathermy coagulating current within the labyrinth and claimed that by doing this they were able to destroy vestibular without interfering with cochlear function. Intracranial section of the eighth nerve was advocated by Dandy (1928) and section of the vestibular portion only, leaving the cochlear division intact, by McKenzie (1932). Mogan and Baumgartner (1924) excised the stellate ganglion, and recently, division of the vertebral artery combined with stellate ganglionectomy, have been described by Passe and Seymour (1948).

Since 1938 I have been removing all or part of the membranous semicircular canal in cases of Meniere's Disease, and the technique and results in the first 50 cases were described in 1943 (Cawthorne). Further experiences with this procedure were given in 1947 (Cawthorne), and to date I have operated on 159 cases by this method, the technique of which is as follows :—

Under general anæsthesia, the mastoid is approached by either the post-aural or end-aural route. The mastoid antrum is opened widely so as to expose fully the external semicircular canal but without encroaching upon the external auditory meatus. In order to get a proper exposure it is

necessary to remove enough of the outer attic wall to uncover, not only the incus, but also the head of the malleus. The incus is then removed in order to give better access to the lateral semicircular canal. The later stages of the exposure just described are made easier if magnifying glasses (Zeiss-Ullstrom giving 2½ diameters of magnification) are used. Then the bony external semicircular canal is opened widely over its convexity using a dental drill with a diamond paste burr. The wide opening affords a good view of the membranous canal and enables it to be grasped with a pair of fine non-toothed ophthalmic forceps and drawn out.

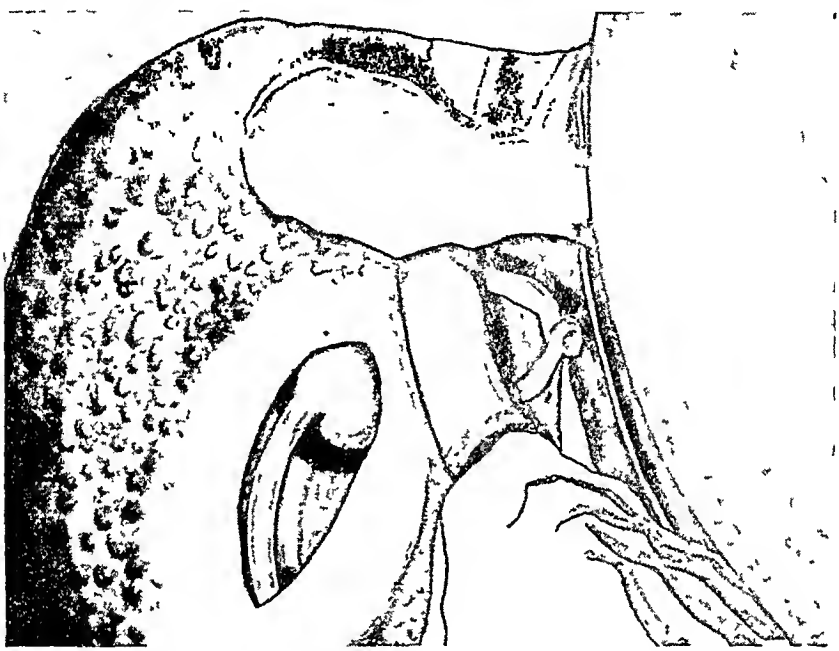


Fig 2. *Labyrinthectomy. Exposure of membranous canal.* Appearance of operative field as seen through binocular dissecting microscope (×10). An opening has been made in the bony external semicircular canal, exposing the membranous canal and its ampulla.

In order to do this part of the operation I have found it advisable always to work in a magnified field, using a Leitz binocular dissecting microscope giving 10 diameters of magnification, having a field of 20 millimetres and a working distance of 22 centimetres. No attempt is made to seal off the opening in the bony canal and the skin incision is sutured without drainage. This is a closed, aseptic operation and prophylactic chemo- or bio-therapy are not essential. In 157 out of 159 cases in which I have employed this technique, healing has been by first intention, and there have been no complications other than those resulting from the sudden loss of labyrinthine function. In the two cases in which infection followed it was easily controlled by chemotherapy—these were before penicillin was available—and both were healed within a week. Out of the 159 cases

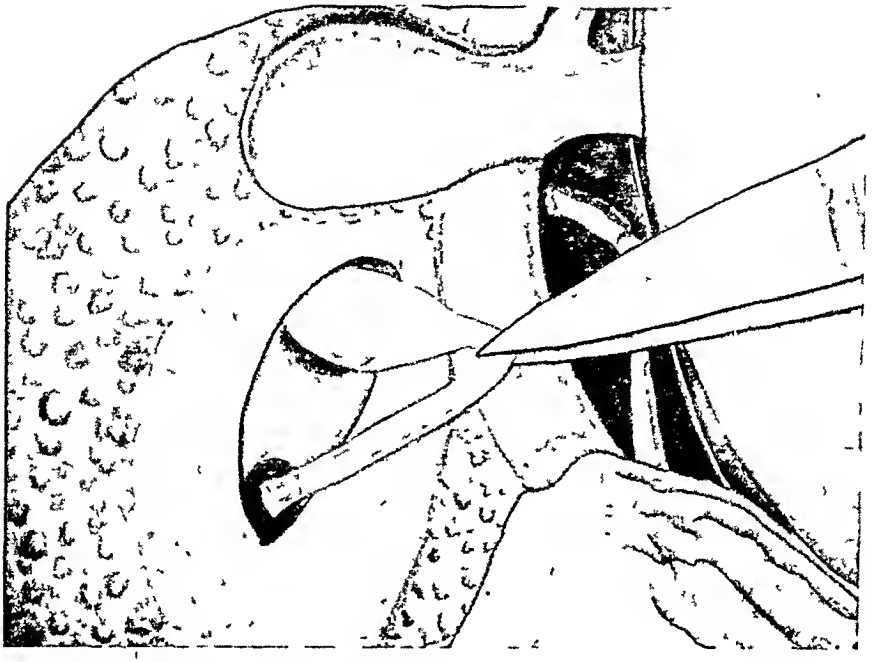


Fig 3. *Labyrinthectomy. Removal of membranous canal.* The membranous external semicircular canal is seized with fine non-toothed ophthalmic forceps and drawn out (× 10).

submitted to operation, 140 were able to return to their former occupations, usually in well under two months.

The following Tables show the immediate and late results of the operation just described :

LABYRINTHECTOMY—IMMEDIATE RESULTS

| | |
|---|---|
| Total Operations .. .. .. .. | 159 |
| Healed by First Intention .. .. .. | 157 |
| Post-Operative Infection .. .. .. | 2 |
| Other Complications .. .. .. .. | 0 |
| Deaths .. .. .. .. .. .. | 0 |

LABYRINTHECTOMY—LATE RESULTS

| | |
|---|---|
| Total Operations .. .. .. .. | 159 |
| Cochlear and Vestibular Function abolished .. | 152 |
| Improved and Able to Work .. .. .. | 140 |
| Not Improved and Unable to Work .. .. | 12 |
| No Record .. .. .. .. .. | 7 |

Though technically not easy, it is, in terms of general surgical principles, simple. That is to say, sufficient of the affected organ is removed to destroy disordered function. Freedom from complications is attributed to the fact that vital structures are not involved, that it is an aseptic

operation, and that nothing that may be harmful to body tissues is introduced into the perilymphatic space or adjacent structures.

This operation is followed by a total and irreversible loss of both cochlear and vestibular function on the affected side. The principal disadvantage to it is that potentially useful hearing is sacrificed. It must be borne in mind, however, that Meniere's Disease affects cochlear as well as vestibular function, with the result that, in addition to the hearing being impaired, it is also, as a rule, distorted particularly for musical sounds, Cawthorne (1943). Such distortion may be very distressing to a patient and, if the hearing in the other ear is normal, is a handicap rather than an asset. It is, therefore, I think fair to say that unless there is evidence to suggest that both labyrinths are or may be involved by the disease process—and one of the essential preliminaries to the operation is a careful investigation and assessment of labyrinthine function—there is little to be gained by trying to preserve a distorted remnant of hearing. If there is any reason to suppose that both labyrinths, and I refer particularly to the vestibular labyrinth, are involved, then some other form of surgical treatment, that does not necessarily sacrifice hearing, should be employed. Although it is outside the scope of this paper I should mention that before any form of operation is contemplated, the possibility of obtaining relief by non operative measures should be thoroughly explored. It is my practice to reserve operation for those patients whose symptoms cannot be controlled by conservative forms of treatment of proven value.

## REHABILITATION AFTER OPERATION OR INJURY

The most disturbing sequel of a labyrinthine injury is vertigo. In its acutest form it has been vividly compared with being simultaneously seasick and in an earthquake. Fortunately such sensations quickly subside but, if the vestibular labyrinth has sustained permanent injury, there will remain, possibly for a long time, some instability of balance. This is particularly noticeable after sudden movements of the head, walking up or down stairs, or on an uneven or inclined surface, or moving about in the dark, or watching rapidly moving objects. There is also a tendency to tire easily on exertion.

The significance of these symptoms and their relief can be better understood if we consider the mechanism of the sense of balance; for it is one of the senses though not included in the traditional five. Balance is maintained as the result of impressions received from the eyes, the skin-muscle-joint sense, and the vestibular labyrinth. In everyday life man is accustomed to rely on his eyes and skin-muscle-joint sense for ordinary balance, while the activity of his vestibular labyrinth is available to take command of skeletal muscular movements if necessary. Any impairment of vestibular activity will upset the pattern and disturb balance; though if the impairment is constant as in a labyrinthine injury rather than fluctuating as in hydrops, then it is possible gradually to adjust the

balancing mechanism to the altered circumstances. In the same way partial or complete failure of one engine in a twin or multi-engined aeroplane can, after the initial disturbance, be compensated by a suitable adjustment of the controls by the pilot, though thereafter the steadiness of the flight is more easily disturbed by outside influences.

Lack of appreciation of the sequelæ of a labyrinthine injury—particularly if it is unsuspected as in post-concussive conditions—may lead the patient to fear a more serious cause; and the doctor, in the absence of any familiar and easily demonstrable signs of disorder, to overlook the organic cause and lay the blame on a psychological disturbance. This combination of circumstances leads naturally to a neurotic state that may further complicate the picture.

The first step, then, in any scheme of rehabilitation is to see that the patient understands the true nature of the disturbance and, in the case of deliberate operative injury, to warn him beforehand of what is going to happen. Recovery of balance is hastened by the use, preferably in a class, of graduated exercises designed to encourage eye, head, and body movements, Cawthorne (1945), Cawthorne and Cooksey (1946).

A graduated series of exercises was developed in the Physiotherapy Department of King's College Hospital and they play a leading part in restoring patients who have sustained a labyrinthine injury to a normal life. A definite scheme of progression is followed, the exercises being done first of all in bed, then sitting, then standing, and then moving about on the flat, and finally up and down stairs and inclined planes. Exercises are done first with the eyes open, then closed and the following scheme includes a specimen series of the exercises.

## THE SCHEME OF EXERCISES

AIMS:

(1) To loosen up the muscles of the neck and shoulders; to overcome the protective muscular spasm and tendency to move "in one piece."
(2) To train movement of the eyes independent of the head.
(3) To practise balancing under everyday conditions with special attention to developing the use of the eyes and muscle and joint sense.
(4) To practise head movements that cause giddiness and thus gradually overcome the disability.
(5) To become accustomed to moving about naturally in daylight and in the dark.
(6) Generally to encourage the restoration of self-confidence and easy spontaneous movement.

PROGRESSION:

Following operation of the labyrinth these exercises may be started in bed on the third day. By the sixth post-operative day most patients can

join the gymnasium class for sitting exercises in a wheel-chair, progressing to standing exercises on the eighth day. For other cases progress will be governed by the general condition of the patient.

All exercises are started in slow time and gradually progress to quick time. The rate of progress from bed to sitting and then to standing exercises depends upon each individual case, and the times mentioned for post-operative cases represent the average. It has been found that class exercises encourage a steady rate of progress.

EXERCISE TABLE:

(A) *In Bed*:
- (1) Eye movements—at first slow, then quick.
  - (*a*) Up and down.
  - (*b*) Side to side.
  - (*c*) Focusing on finger moving from 3 feet to 1 foot away from face.
- (2) Head movements at first slow, then quick. Later with eyes closed.
  - (*a*) Bending forwards and backwards.
  - (*b*) Turning from side to side.

(B) *Sitting* (in class):
- (1) and (2) (A).
- (3) Shoulder shrugging and circling.
- (4) Bending forwards and picking up objects from the ground.

(C) *Standing* (in class):
- (1), (2) and (3).
- (4) Changing from sitting to standing position with eyes open and shut.
- (5) Throwing a small ball from hand to hand (above eye level).
- (6) Throwing ball from hand to hand under knee.
- (7) Change from sitting to standing and turning round in between.

(D) *Moving About* (in class):
- (1) Circle around centre person who will throw a large ball and to whom it will be returned.
- (2) Walk across room with eyes open and then closed.
- (3) Walk up and down slope with eyes open and then closed.
- (4) Walk up and down steps with eyes open and then closed.
- (5) Any game involving stooping or stretching and aiming such as skittles, bowls and basket-ball.

Detailed exercises in the scheme outlined above can be varied or extended according to need. The order in which the exercises are carried out should not as a rule be changed.

The stimulating effect of example and competition that is seen when these exercises are done in a class further hastens recovery, and it is usually found that two or three weeks of exercises are sufficient to set most patients well and truly on their feet again. They are not intended for cases

of Meniere's Disease except after operation, not for other forms of fluctuating vertigo. When, however, there is some constant loss of function in one or other labyrinth, then the exercises hasten the restoration of balance and encourage the patient to overcome the slight momentary dizziness provoked by sudden head movements.

They form part of the routine after treatment of every labyrinthine operation, and any case of head injury followed by vertigo. They can also be used with advantage for any case of permanently impaired vestibular function, whether the result of operation, injury or disease.

In conclusion I would like to thank all my friends and colleagues at the National Hospital for Nervous Diseases, Queen Square, King's College Hospital and elsewhere for referring their cases of vertigo to me. In particular I would like to record my indebtedness to Dr. C. S. Hallpike and Dr. F. S. Cooksey whose constant advice and co-operation made this work possible. Finally I would like to thank my friend Mr. A. B. Hewlett for his assistance and support in every aspect of this work, and in particular for the drawings that are included in this paper. I feel sure that he will agree with me in attributing our initial interest in the labyrinth to what we learnt from our former teachers at King's College Hospital, A. H. Cheatle and G. J. Jenkins.

## REFERENCES

ALTMANN, F., and FOWLER, E. P., jr. (1943) *Ann. Otol. etc., St. Louis* **52**, 52.
ATKINSON, M. (1941) *J. Amer. med. Ass.* **116**, 1753 ; *Arch. Otolaryng.* **4**, 385.
BAGINSKY, B. (1881) *Arch. Physiol., Lpz.* 210.
BARANY, R. (1906) *Mschr. Ohrenheilk* **50**, 229.
BARMOEL and MARKS (1941) *Arch. Otolaryng.* **33**, 204.
BARRE, J. A., and GREINER, G. (1932) *Rev. Oto. Neuro. Ophthal.* **10**, 633.
BERGGREN, E. (1939) *Act. Otolaryng.* **27**, 626.
BREUER, J. (1874) *Wien Med. Jahr.* **4**, 72.
BRUNNER, H. (1928) *Alexander und Marburg Handbuch der Neurol. des Ohres.* **2**, pt. 1. 273.
——————— (1940) *Laryng.* **50**, 921.
CAWTHORNE, T. (1943) *J. Laryng.* **58**, 363.
——————— (1945) *J. Chart. Soc. Physioth.* April.
——————— (1947) *Ann. Otol. etc., St. Louis* **56**, 18.
——————— and COOKSEY, F. S. (1946) *Proc. Roy. Soc. Med.* **39**, 270.
——————— and FAWCETT, M. (1938) *Lancet* **2**, 1404.
——————— FITZGERALD, G., HALLPIKE, C. S. (1942) *Brain* **65**, 161.
CROCKETT, E. A. (1914) *Tr. Amer. Otol. Soc.* **13**, pt. 2. 302.
CROWE, S. J. (1938) *Medicine, Baltimore* **17**, 1.
CRUM-BROWN, A. (1875) *J. Anat. Physiol.* **8**, 327.
DANDY (1928) *Arch. Surg.* **16**, 1127.
DAY, K. (1943) *Laryng.* **53**, 617.
DEDERDING, D. (1929) *Acta Otolaryng.* Suppl. X-XI.
DENNY BROWN, D. (1943) *Ann. Intern. Med.* **19**, 427.
——————— and RUSSELL, R. (1941) *Brain* **64**, 93.
DOHLMAN, G. (1939) *Acta Otolaryng.* **27**, 245.
DUKE, W. W. (1923) *J. Amer. med. Ass.* **81**, 2179.

EWALD (1892) *Physiologische Untersuchungen über das Endorgan des Nervus Octavus.* Wiesbaden.

FLOURENS, P. (1824) *Recherches experimentales sur les propriétés et les fonctions du système nerveux dans les animaux vertebrés.* Paris. Baillière.

FURSTENBERG, A. D., LASHMET, F. H., LATHROP, F. (1934) *Ann. Otol. etc., St. Louis* **43**, 1035.

GLASER, M. A. (1937) *Ann. Otol. etc., St. Louis* **46**, 387.

HALLPIKE, C. S. and CAIRNS, H. (1938) *J. Laryng.* **53**, 625.

——————— and WRIGHT, A. J. (1940) *J. Laryng.* **55**, 59.

HAUTANT, A. (1934) *Bull. Acad. Med.* **111**, 933.

JENKINS, G. J. (1911) *Proc. Roy. Soc. Med. Otol. Sect.* 116.

KNAPP and CHEATLE, A. H. Quoted by Fischer, J. and Wolfson, L. E. *The Inner Ear,* New York. Grune and Stratton, 1943.

KRAMER, W. (1948) *Traité des Maladies de l'Oreille.* Trans. by P. Meniere. Paris. Germer-Baillière.

LAKE, R. (1904) (1911) *Lancet,* 1638.

LEMPERT, J. (1938) *Arch. Otolaryng.* **28**, 42.

——————— (1948) *Arch. Otolaryng.* **47**, 551.

LESLIE, S. (1928) *The Skull of Swift.* London, Chatto and Windus.

LINDSAY, J. R. (1942) *Arch. Otolaryng.* **35**, 853.

LINTHICUM, F. H., and RAND, C. W. (1931) *Arch. Otolaryng.* **13**, 785.

LURIE (1944) *Laryngoscope.* **54**, 375.

MCKENZIE, D. (1924) *J. Laryng.* **39**, 446.

MCKENZIE, K. (1932) *Tr. Acad. Med. Toronto,* Nov. 15.

MCNALLY, W. J. (1933) *Tr. Amer. Otol. Soc.* 99, 105.

MACH, E. (1874) *Grundlinien der Lehre von den Bewegungsempfindungen.* Leipzig: Engelmann.

MAGNUS, R. (1924) *Korperstellung.* Berlin. J. Springer.

——————— and DE KLEIJN, A. (1912) *Pflug. Arch. ges Physiol.* **145**, 455.

MENIERE, P. (1861) *Gaz. Med. Paris.* 585.

MILLIGAN, W. (1912) *J. Laryng.* **27**, 521.

MOGAN, R. F., and BAUMGARTNER, C. J. (1934) *West J. Surg.* **42**, 628.

MOLLISON, W. M. (1931) *J. Laryng.* **46**, 191.

MYGIND, S. H. (1918) *Acta Otolaryng.* **1**, 515.

——————— and DEDERDING, D. (1932) *Acta Otolaryng.* **17**, 424.

OHNELL, H. (1932) *Arch. Verdaukr.* **51**, 281 (May).

OSNATO, M., and GILIBERTI, V. (1927) *Arch. Neurol. Psychiat.* **18**, 181.

PASSE, G., and SEYMOUR, J. S. (1948) *Brit. Med. J.* **2**, 812.

PORTMANN, G. (1927) *J. Laryng.* **42**, 809.

PUTNAM, T. J. (1938) *Arch. Otolaryng.* **27**, 161.

ROLLIN, H. (1940) *Z. Hals. Nas. u. Ohrenheilk (Teil* 1.) **31**, 72.

RUSSELL (1932) *Brain* **55**, 549.

SHAKESPEARE, W. (1623) *Julius Caesar, Act I. Sc. II.*

STEINHAUSEN, W. (1931) *Mschr. Ohrenheilk* **29**, 211.

SYMONDS, C. P. (1937) *Guy's Hosp. Gaz.* **51**, 461.

——————— (1943) *Injuries of Skull, Brain, and Spinal Cord.* Ed. S. Brock. Baltimore, Williams p. 65.

TEMKIN, O. (1945) *The Falling Sickness.* J. Hopkins Press, Baltimore.

VOSS (1934) *J.A.M.A.* **103**, 1721.

WILLIAMS, H. L. (1944) *Ann. Otol. etc., St. Louis* **53**, 397.

WRIGHT, A. J. (1937) *Proc. Roy. Soc. Med.* **31**, 87.

# SURGICAL PROBLEMS INVOLVED IN BREAST CANCER

Moynihan Lecture delivered at the Royal College of Surgeons of England

on

23rd March, 1949

by

Frank E. Adair, A.B., M.D., F.A.C.S. (Hon.) D.Sc. (Hon.), LL.D.
Attending Surgeon, Memorial Hospital, New York

TO ANY AMERICAN it is a rare and distinct honour to be invited to address the Royal College of Surgeons of England and, to your distinguished President and Council of the College, I am deeply grateful for this privilege.

It must give a warm sense of glow to every member of England's Royal College of Surgeons to look backwards over the 150 years of its existence and to contemplate the great accomplishments of its individual members. The roots of your College, embedded in the John Hunter Museum, had rich soil in which to develop. Your long list of famous lecturers included, among others, the names of Laurence, adumbrator of Darwinism, Abernethy, Owen, Huxley, Sir Astley Cooper, George Murray Humphrey and Sir Arthur Keith, the anatomist.

Your museum, a shrine to men of science the world over, although badly damaged by enemy action during World War II, will eternally bear the names of giants—John Hunter, Towne and Sir James Paget. The name of Lord Lister is engraved on the mind of every school child.

The importance of your College in the life of science and in the development of the medical profession can never be fully measured. The history of the College is literally revered throughout the world.

I would seem ungrateful were I not to at least touch for a moment on the great debt that American surgery owes to English surgeons. At the beginning of the nineteenth century the young American wishing a medical education journeyed either to London or Edinburgh.

Philip Syng Physick came to London from America in 1789, became a pupil of John Hunter, and served as his house surgeon at St. Georges Hospital. Physick later became known as the "Father of American Surgery," for his great leadership and influence at and beyond the walls of the University of Pennsylvania.

I am impelled to speak of the strong bonds which have existed between your College, and the young American College of Surgeons, now in its thirty-sixth year. As a medical student, I had the opportunity of meeting your then President, Sir Rickman Godlee, the nephew of Lord Lister, when he came to Johns Hopkins Medical School, the guest of our first President of the American College of Surgeons, Dr. John M. T. Finney. Godlee, as President of your College, had come to America to represent the Royal College of Surgeons of England at the founding of the American College of Surgeons in 1913.

The great gold mace later presented to the American College of Surgeons at one of its convocations by the Surgical Consultants of the British Army of World War I, was brought to America by a group headed by your then President, Lord Moynihan. The mace embodies the faith of British surgeons in the future of the American College of Surgeons, and it also is a beautiful symbol of mutual helpfulness in peace and war. The mace is in evidence at every formal meeting of our College, and is always a reminder of our belief in each other. As a Governor of the American College of Surgeons for a good many years, and as Chairman of its Cancer Committee for 10 years, I acknowledge with due humility, the great debt we owe you.

It is unusual for an American surgeon to have had the opportunity of meeting three presidents of the Royal College of Surgeons of England. I have had that pleasure in meeting Godlee, Moynihan, and Webb-Johnson. And this brings me to speak of Lord Moynihan, in whose honour this lectureship is named. I especially appreciate being given the opportunity of giving the Moynihan Lecture. Moynihan had an enormous interest in cancer. He was most effective in helping to build up the Yorkshire Cancer Campaign. Moynihan had greatness as a man; he had daring and skill as a surgical *technician*; but he also had rare ability as a medical writer and expressed himself with lucidity and, at the same time, great charm. I well remember once, while he was attending a staff conference at our hospital in New York City, Lord Moynihan stated: "I have been so impressed with the work of Geoffrey Keynes with his radium needles, that I doubt if I shall again do another radical mastectomy; however, I may." To-day, I believe Moynihan would have sufficient statistical evidence to persuade himself that surgery is still the tool on which he could best rely; in spite of that brilliant work of Keynes.

This statement in 1929 made a great impression on many of us, especially on Ewing, the distinguished pathologist, who was constantly on the alert for some effective substitute for the scalpel.

During the nearly 30 years of my interest in breast cancer, I have constantly seen complete reversals take place in viewpoints toward the problems.

## CLINICAL MATERIAL

All the clinical material in our hospital is divided into the major types of clinical cancer, and around each classification a staff is built to produce men who have an unusually big experience and, incidentally, knowledge of a particular type of cancer, including its experimental aspects, its surgery, its irradiation therapy by radium and X-rays, and its other chemical phases which may have a place in its complete, rounded study. Credit or discredit for such a division of clinical material must go to Ewing. In his defence one must only point to the record growth of each of the clinical departments of our hospital.

Professor Burton J. Lee and I started the Breast Department in 1920, and since 1933 I have been in charge of it.

The following will give an idea of the clinical activities for the year 1948 :

| | |
|---|---|
| New Breast Cases Admitted to the Department .. | 1,860 |
| Radical Mastectomies .. .. .. .. .. | 631 |
| Local Excisions of Breast Tumours and Areas of Local Pathology .. .. .. .. .. .. | 1,113 |
| Total Breast Operations .. .. .. .. .. | 1,792 |
| Follow-Up Visits .. .. .. .. .. .. | 13,527 |
| X-Ray Treatments .. .. .. .. .. | 14,451 |

Our experience, philosophy, and conclusions are based on the care and study of 13,054 cases of breast cancer at the Memorial Hospital. Our cases of cancer of the breast are divided and classified as follows :

| | *Number of Cases* |
|---|---|
| Primary operable .. .. .. .. .. .. | 8,025 |
| Operable after local excision elsewhere .. .. | 598 |
| Primary inoperable .. .. .. .. .. | 1,727 |
| Recurrent inoperable .. .. .. .. .. | 1,824 |
| Prophylactic .. .. .. .. .. .. | 707 |
| Sarcoma .. .. .. .. .. .. .. | 48 |
| Male breast cancer .. .. .. .. .. | 125 |
| | 13,054 |

Of our 13,054 cases of breast cancer, 66 per cent. were considered operable. Our material to-day, however, is running at a higher percentage of operability—approximately 75 per cent.

## INCIDENCE

The race in which we find the highest percentage of breast cancer is the Hebrew race. At present there is no explanation which is entirely acceptable to all. However, among the reasons given are the following :

(1) As carcinoma of the cervix uteri is so very rare in Jewish women, it has been stated that they numerically make up for this lack of cervix carcinoma, by greatly increasing the amount of breast carcinoma. This gives no reason as to why this condition exists.

(2) It has been stated that the reason Jewish women do not often get cervix carcinoma, is that the religious rites of circumcision are meticulously carried out and consequently that there is less opportunity for carrying infection up to the cervix, which when lacerated and infected is more apt to develop cancer.

(3) The most probable reason, in my judgment, is that in the Hebrew, we are dealing with an inbred race, rarely marrying outside their own people, which could easily explain it along well recognized laws of genetics and heredity.

## HIGH SELECTIVITY

There are few fields of science where there is greater discrepancy and irregularity of evaluating therapy than in the statistics of cancer. The

method by which some investigators arrive at the statistical results of therapy is quite different from that of another group, making it so that comparisons are impossible. Frequently, the conclusions are arrived at by a study of a small number of cases, too few to have statistical significance. Clinicians should not handle the statistics of therapy. That should be done by experts in biometrics; and they, if expert, will insist that every single case in the study be accounted for. One of the most common and inexcusable faults in the study of cancer cases is the selection of good cases to report on and the failure to report on the less favourable cases. One will get the impression that the cure rate is much higher in the hands of a particular clinician than in the hands of another, both doing an equally good operation. There is an enormous difference in clinics as to what constitutes an operable case of breast cancer. If one has to account for what happens to every case, he is less apt to be so highly selective as to operability, because he must still account for those on whom he did not choose to operate. If the unfavourable cases show too low a percentage of cure, while the favourable cases show too high a percentage of cure, it is obvious that too many cases who still have an opportunity for cure are thrown into the group whose therapy is admittedly minimal or only slightly effective.

Our own philosophy is to interpret operability along very generous standards. Realising that there is no means of salvage to be compared with radical surgery, I am apt to give a patient the opportunity of a radical, which in the hands of some clinicians would be denied. I believe this to be correct. Even this broader selection, or what some might call careless selection, has given us the following results:

| | Pre-operative Irradiation Radical Surgery | Immediate Surgery Post-operative Irradiation 628 cases in 1942 |
|---|---|---|
| The five-year salvage in the 3,988 cases (1935 to 1942)—advanced as well as operable cases .. .. .. .. .. .. | 39.6% | 46% |
| 2,159 operable cases (treated by surgery or irradiation, or both) .. .. .. .. | 54.3% | 60.6% |
| 1,913 operable cases (treated by radical surgery) .. .. .. .. .. | 56.2% | 60.2% |
| 737 operable cases (treated by radical surgery) breast alone involved .. .. .. | 78.6% | 83.8% |
| 1,173 operable cases (treated by radical surgery) breast and axilla involved .. .. | 42.2% | 47.2% |

The overall cure rate, including every case—advanced as well as early—was 39·6 per cent.

In the article by Haagensen and Stout (*Annals of Surgery*, Dec., 1943, p. 29) 13 criteria are given which they think indicate inoperability, some singly and some criteria in combination. We fully agree that many of these criteria indicate a poor prognosis ; but who has not been mistaken in his clinical estimate of a case ? Who has not obtained a cure in a case when he had anticipated a failure ?

One of their criteria of inoperability is ulceration. I do not agree that ulceration of the carcinoma *per se* should always indicate inoperability. It is well known that adenocarcinoma of the breast ulcerates comparatively early in its course, due to pressure necrosis against the overlying skin. We once had an adenocarcinoma of the breast which had been ulcerated for 10 years. Curiously enough, at the radical operation, no node was found to be involved with cancer. We therefore have a viewpoint of ulceration quite different from these authors.

Pregnancy and lactation were also both contra-indications for the radical operation in their list. Obviously, they offer a poor prognosis ; but it is unthinkable, to me, that every case of pregnancy or lactation, accompanied by a breast cancer, should be thrown out of consideration for cure. Recently, in going through the records of 27 patients with pregnancy in whom cancer of the breast developed, we found seven, or 25 per cent., who had survived five years or more, following the radical.

With them, I agree as a rule on the contra-indication of supra-clavicular metastasis ; however, there is a growing modern tendency to extend the frontiers of surgery in breast cancer. If the chest plate is negative, and the involvements of the supra-clavicular area is minimal, I think it is often justified to split the clavicle or remove it and extend the operation on up into the base of the neck. A few years ago Semken presented three cases of breast cancer with supra-clavicular involvement, who survived from six to nine years after radical mastectomy, accompanied by neck dissection.

Anyone who carefully excludes from operation every case with an apparent poor prognosis, should have a very high percentage of cure closely approaching 100 per cent. by radical mastectomy of his highly selected material. I consider this not meeting our full responsibility as clinicians. We must insist on the report of survivals of the other material which was excluded from operation.

## BIOPSY

Biopsy in breast tumours is a necessary evil. I do not minimize its possible hazards, either on theoretical or practical grounds. An excisional biopsy carelessly performed can easily be a definite hazard, and it is not a difficult matter to get so close to the tumour, as to accidentally cut into it while performing the excision. Furthermore, if the tumour be cancer, it is a fact in every case that lymphatic channels between the tumour and the axilla will be cut across ; and on every theoretical ground this is wrong. Practically, however, biopsy is necessary, and cannot be avoided until some new development occurs, such as the deposit in the tumour

of an isotope which is revealed by the Geiger counter, the use of fluorescine as revealed by a violet light, similar to its use in brain tumours, or some other entirely new method of obtaining the desired information.

The following are the methods of biopsy usually employed in breast tumours :

(1) Excisional Biopsy.
(2) Incisional Biopsy.
(3) Aspiration Biopsy.

To my mind, aspiration biopsy is the best method if the tumour is easily accessible—which it frequently is. Next in order, I prefer the total excision of the tumour with a good margin of surrounding tissue ; and least of all, I like the incisional biopsy method of cutting directly into the tumour and removing a small portion.

### 1.—Excisional Biopsy

A total excision of the tumour in question, together with a good zone of surrounding breast tissue, is one of the best types of biopsy as it gives the pathologist a satisfactory specimen for his frozen section. One should not make a single incision directly over the tumour. Many times (and this can be microscopically demonstrated), there are cancer cells in the lymphatics of the suspensory ligaments leading up from the breast to the overlying skin ; it is therefore preferable to make two skin incisions, removing the skin overlying the tumour.

There is also another procedure which is helpful. Following the making of the two skin incisions, one should pull the mass containing the tumour laterally, making the dissection rather widely down to the pectoral fascia through the breast substance. One can then place two or three fingers behind the specimen, lift it upwards, and immobilize it so that the removal is facilitated ; and the excision made more accurate.

### 2.—Incisional Biopsy

The removal of a portion of the cancer for microscopic examination offers certain dangers of dissemination that do not exist to the same extent in the other two types of biopsy. By cutting directly into the tumour, bleeding immediately starts, and during the process of removing the piece of cancer, the lymphatic spaces and blood vessels are opened, and the cancer cells are manually pushed into the open spaces during the inevitable procedure of sponging, necessary in order for the operator to see the field. The knife, hemostats, and retractors have scattered cancer cells over their surface, and the wound, including the skin immediately surrounding the wound, also have cancer cells present. This method of biopsy therefore should not be employed except when absolutely necessary as the danger, not only of immediate distant metastasis is real, but it offers a greater possibility of local recurrence than other methods.

### 3.—Aspiration Biopsy

Aspiration biopsy is a form of biopsy originally developed by Martin, Ellis and Stewart at the Memorial Hospital. The method is simple, and

has the great advantage of speed in obtaining a diagnosis. It also has the important advantage of saving a patient from an additional half-hour of anæsthesia and operation, which are so vital in bad risk patients. Some develop high skill in its performance. The technique is simple. The equipment necessary is a tiny needle for injection of novocaine into the skin, a fine point knife to make a prick in the skin, so the needle is not gripped by the skin, a tight fitting record syringe with an 18 gauge needle, and a needle stylette to push out the cell droplet, obtained by aspirating the tumour, on to a glass slide. Another glass slide is then placed on top of the tissue droplet and a smear made of the material. The slides are then stained and read by the pathologist. The technical procedures can be done easily and the pathologist can give you a diagnosis within 10 minutes. Most pathologists, without experience in this technique, will object at first; however, after a month of instruction under an expert, they get more confidence and become a great help to the clinician. It therefore has the advantages of speed in diagnosis, and of minimizing the amount of procedure necessary to obtain a diagnosis. It also saves the re-painting, re-draping, re-gowning and re-gloving. Aspiration biopsy is, as a rule, performed before the patient comes to the operating room. In our hospital aspiration biopsy is practised commonly on many types of cases, including neck nodes, lymphosarcoma nodes, breast tumours, bone tumours, chest wall tumours, lung tumours, liver tumours, and other areas, where we think the risk is not too great.

Some surgeons attain a high degree of skill in obtaining material by aspiration. One resident surgeon obtained a positive diagnosis of cancer by aspiration in 96·5 per cent. of his aspirations of cancer of the breast.

Of 1,579 cases of breast carcinoma during the past five years, in which this form of biopsy was performed, 806 were done by my resident surgeons with experience in this work, having 80 failures (9·9 per cent.) obtaining a correct diagnosis of 90·1 per cent. Of the 773 cases of breast cancer in whom the aspiration biopsy was performed by doctors new to the technique there were 156 failures (20 per cent.); or 80 per cent. were correct.

I must state that included in these failures are cases where the tumour was situated so deep, or was so small, that that particular case was not one which should be considered fair to an estimate of this method. On the other hand, we have many times been greatly surprised to obtain a positive report when we assumed beforehand that we would not. Every case does not loan itself equally to this method of biopsy, but it has a most useful place in breast tumours.

It should be obvious that a negative report of cancer in an aspiration biopsy indicates nothing except that the surgeon will have to take the patient to the operating room and perform a formal surgical biopsy.

The advantages of aspiration biopsy are numerous and obvious, if there is co-operation between pathologist and surgeon. It also has

certain disadvantages. If the tumour is extremely hard it is at times not easy to obtain a tissue droplet. Metastatic areas in bone are, however, constantly being diagnosed by this method. There is a possibility, if careless, of pushing the needle through the cancer into deeper tissues. We have seen the tissue droplet, when smeared and diagnosed, reveal muscle or cartilage, indicating that one had gone too deep. In one case where the aspiration biopsy was carelessly done the patient even received a pneumothorax.

## EXTENSION OF SURGERY

There are certain areas where one might reasonably consider the extension of radical surgery in breast cancer. With present-day assistance which we get from the injection of large quantities of whole blood, plasma, penicillin, proteids, phosphorus and calcium, the frontiers of radical surgery have been pushed back and we, to-day, dare attempt operations which were previously denied us.

There have been many efforts during the past 50 years to develop substitutes for surgery in mammary cancer, such as X-ray and radium therapy, the cautery, electro-coagulation, and hormones, but, in my opinion, no effective substitute for meticulous radical surgery has yet been developed. In fact, the trend to-day is even toward more extensive surgery for cure and palliation. Considerations are before us such as the following:

(1) Extending the classic operation to include nodes at the base of the neck.
(2) Removal of the clavicle for greater exposure.
(3) The removal of the nodes along the internal mammary artery.
(4) The removal of ribs involved by breast cancer.
(5) The routine removal of the axillary vein.
(6) An inter-scapulo-thoracic amputation, sweeping off neck and axillary nodes.

There is one thing which I feel strongly, that the substitution of the radical mastectomy by simple mastectomy and the addition of irradiation therapy, is costly in lives and wrong in principle because irradiation therapy will not cure mammary cancer with any degree of consistency, particularly in the axilla where it may cause necrosis of one involved node and leave completely viable a similar node which received the identical amount of irradiation.

In the beginning of the radical mastectomy in 1893 Halsted then combined in some cases the radical mastectomy with the neck operation. At that time the radiograph had not yet been developed, so it was not possible to ascertain the status of lungs for the presence of metastasis. After a time Halsted gave up the neck operation first, because of high

operative mortality, and next because he came to the conclusion that if there was positive supra-clavicular involvement there was also disease in the chest. A study of the lymphatic system reveals that most of the breast drains its lymphatic contents into the base of the axilla ; however, it is known that the upper inner quadrant of the breast drains not only into the axillary nodes, but there are some lymphatic channels which drain directly anterior to the clavicle and into the supra-clavicular nodes. Therefore in that case, having its cancer so situated, if its supra-clavicular nodes were involved with disease, it could conceivably be successfully reached and cured.

Cancer as a rule metastasises first into the base of the axilla (Group I nodes), it then extends along the subclavian vein to the axis group behind the pectoralis minor (Group II nodes), it extends from there into three possible directions : (*a*) medially to nodes at the falciform ligament (Group III nodes) ; (*b*) extension upward into the base of the neck ; and (*c*) into the sulcus along the high mediastinum. We already have the information that it is occasionally possible to effect a cure if a low neck dissection is done. This is a matter of record. On the other hand, one must judiciously consider the advisability of such an extensive procedure, as one must balance the total sum of additional lives salvaged, against those lost by this combined surgical procedure. It is the rare case which loans itself to an extension of the radical mastectomy on up to include the low neck nodes. However, this setting at times does exist in the absence of lung metastasis. And it is in this case that the middle half of the clavicle or the entire clavicle may be removed and a block dissection of the low neck nodes made, sweeping the tissue downward in continuity, together with all tissues of the axillary and breast specimens. The deformity of the shoulder and arm is less than anticipated, and the function is good.

It has been suggested by Neuhof (Neuhof, H. : Excision of axillary vein in the radical operation for carcinoma of the breast. *Annals of Surgery* 108 : 15-20, 1938) several years ago, that the axillary vein be routinely removed at radical mastectomy. More recently MacDonald (MacDonald, Ian : Resection of the axillary vein in radical mastectomy. *Cancer*, Vol. I, No. 4, p. 618) has advocated the routine *en bloc* removal of the axillary vein and its surrounding fat and lymphatic tissue. This procedure of Neuhof and of MacDonald, although adding to the more complete cleaning out of the axilla, certainly as a routine procedure, brings up for consideration the investigation of the competency of the cephalic vein in very case before one dares carry it out.

Occasionally in a case where the lungs are negative, and when there is involvement of the nodes of the low neck; an inter-scapulo-thoracic amputation is thoroughly justified. We think this operation especially useful in those cases where radiation damage to supra-clavicular skin is painful in the presence of disease. By this procedure the nodes of the lower neck, together with all lymphoid and fat tissue, the clavicle, scapula

and arm, will be swept off cleanly from the first and second rib area. This is admittedly a drastic procedure, but there are certain urgent instances where, for special reasons, this procedure is more than justified; and where the life of an otherwise doomed patient may be salvaged.

## MILK FACTOR

The easiest explanation of the hereditary factor if it could be proven, would be the existence of a milk factor in the human, similar to that proven in the mouse. However, my own efforts at proving the existence of a milk factor in the human have not proven its existence. The difficulty of establishing the milk factor is that in so comparatively few cases is it possible to get critical information as to whether the mother nursed the child, whether the grandmother nursed her child, &c. Human lives last so long to-day that it is difficult to establish in a given case of a woman who developed breast cancer, that she, as a baby, was breast fed. Such a study, to be valuable, would of necessity have to cover a long number of years. Fifty per cent. of my cases studied had been breast fed, and 50 per cent. had not, leaving us with no evidence.

On the other hand, the existence of a milk factor in mice has been so firmly established by both Little and by Bittner, that we must accept the idea. And it gives us all a thrill to realise that with the discovery of the milk factor a virus-like body in the milk of inbred strains of laboratory mice, that Bittner has been able to develop an anti-body against the development of breast cancer in the mouse. This comparatively recent discovery has shed a new ray of hope on the possible future control of breast cancer, if it were possible to transfer the idea to the human. Although this virus-like body can be established in mice, efforts to prove its existence in either rats or the human, have as yet failed.

## HEREDITY

Anyone who has had the opportunity to study large numbers of human cases of breast cancer will sooner or later be impressed with the presence of an hereditary factor. It will not hold good in all cases, but the occasional case exhibits the hereditary aspect most strikingly. A few years ago, in my hospital ward, there were two instances of mother and daughter, all with breast cancer. All were there at the same time. We have had in our care a mother and four daughters, all of whom developed breast cancer at about the same age—46 years. The hereditary influence in breast cancer is so common that it no longer impresses us. It is our observation that this influence is through the maternal side of the family rather than through the paternal side. We have also been interested with its presence in identical twins.

## END RESULTS

Due to great improvements in our records, a consideration of material for this paper will not be made prior to 1932. Our study of 7,394 cases

will be limited to mammary cancer in women only, between January 1, 1932, and December 31, 1947. However, as we cannot report five-year follow-up on cases later than December 31, 1942, it further reduces the cases to 3,988.

TABLE I

FIVE-YEAR SURVIVAL RATES AMONG PATIENTS WITH BREAST CANCER ADMITTED FROM 1935 THROUGH 1942, INCLUDES ALL CANCER CASES, ADVANCED AS WELL AS EARLY CASES

| | | SURGERY | | | PRE-OPFRATIVE IRRADIATION AND SURGERY | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 1942 | 1941 | 1940 | 1939 | 1938 | 1937 | 1936 | 1935 |
| TOTAL NUMBER OF PATIENTS .. .. | 3,988 | 628 | 618 | 611 | 458 | 455 | 428 | 436 | 354 |
| INDETERMINATE GROUP: | | | | | | | | | |
| Applied after treatment elsewhere—no evidence of cancer .. .. .. | 152 | 31 | 14 | 25 | 23 | 19 | 14 | 14 | 12 |
| Consultation only—no treatment .. | 28 | 3 | 2 | 2 | 3 | 2 | 7 | 6 | 3 |
| Patient refused treatment or palliation | 235 | 35 | 49 | 26 | 20 | 32 | 23 | 26 | 24 |
| Dead within five years of other causes without recurrence .. .. .. | 131 | 24 | 23 | 24 | 17 | 8 | 11 | 13 | 11 |
| Lost track of within five years without recurrence .. .. .. .. | 87 | 29 | 16 | 13 | 4 | 11 | 8 | 2 | 4 |
| Total indeterminate results .. | 633 | 122 | 104 | 90 | 67 | 72 | 63 | 61 | 54 |
| DETERMINATE GROUP (Total number minus indeterminate group) .. | 3,355 | 506 | 514 | 521 | 391 | 383 | 365 | 375 | 300 |
| Percentage surviving five years .. | 39.6 | 46 | 438 | 44 | 386 | 366 | 37.3 | 30.1 | 34.0 |
| Primary operable cases (Determinate); some were treated by irradiation only .. .. .. .. .. | 2,159 | 348 | 360 | 349 | 255 | 245 | 218 | 221 | 163 |
| Percentage surviving five years .. | 54.3 | 60.6 | 55 | 57.3 | 52.9 | 53.4 | 55. | 43 | 50.3 |
| Primary operable cases treated by Radical Mastectomy (Determinate) | 1,913 | 329 | 337 | 329 | 222 | 211 | 180 | 179 | 126 |
| Percentage surviving five years .. | 56.2 | 60.2 | 55.2 | 58.4 | 54.5 | 56.9 | 58.3 | 47.5 | 54.8 |
| Primary operable cases treated by Radical Mastectomy (Determinate); breast alone involved .. .. | 737 | 117 | 126 | 127 | 89 | 73 | 85 | 73 | 47 |
| Percentage surviving five years .. | 78.6 | 83.8 | 82.5 | 80.3 | 68.5 | 89 | 75.3 | 63 | 82.9 |
| Primary operable cases treated by Radical Mastectomy (Determinate); both breast and axilla involved .. | 1,173 | 212 | 211 | 202 | 132 | 138 | 93 | 106 | 79 |
| Percentage surviving five years .. | 42.2 | 47.2 | 38.9 | 44.6 | 45.5 | 39.9 | 41.9 | 36 | 37.9 |

Table I gives the complete analysis of the 3,988 cases analysed by years. It is obvious that those cases treated (1935 to and including 1939) by pre-operative irradiation followed by the radical mastectomy were not as successfully treated as the 1940, 1941, and 1942 cases where immediate radical was followed by post-operative X-ray therapy in those cases having axillary involvement.

When Table I is analysed it is noted that the 329 primary operable cases of 1942 treated by the radical mastectomy yielded the following five-year survivals:

| | |
|---|---|
| Breast alone involved .. .. .. .. .. | 83·8% |
| Breast and axilla involved .. .. .. .. | 47·2% |

This brings one to a point which in my view is timely for consideration. In the reporting of end results of therapy, each investigator has

different criteria for the handling of his material; some report five-year survivals; some report five-year cures, meaning those cases are free of recurrence as far as the doctor can ascertain; some report 10- and 15-year survivals. A congress of competent medical statisticians from all over the world should meet, study the different viewpoints and arrive at an acceptable conclusion as to the proper way to statistically handle cancer material. In my own case, all the figures are arrived at by the statistical department, a new branch in the hospital. We, as surgeons, ask that certain statistical problems be developed, but have no personal part in their development.

There is a great difference in the life history of different types of cancer as to recurrence. For instance, cancer of the lip, skin, cervix uteri, stomach, lung, &c., have in common the fact that if there is no demonstrable disease at the end of five years, cure is usually assured in these cases. Their survival curve at the end of the five years does not continue to drop, but straightens out. On the other hand, melanoma of the eye is peculiar unto itself. Following enucleation of the eye for melanoma, metastasis often takes place in the liver 25 to 30 years later.

Likewise, cancer of the breast has a recurrence and metastasis rate peculiar to itself. At the end of five years of freedom from recurrence or metastasis, there is still a 10 to 11 per cent. cancer fatality in those cases which were free from disease at the end of five years. On further analysis of this problem, one is astonished to realise that in those operable cases with axillary lymph node involvement, the rate of subsequent death from cancer goes up to 24·1 per cent. in those cases operated on 16 years previously. (See Table II.)

TABLE II

PERCENTAGE OF PATIENTS FREE OF DISEASE AT FIVE YEARS WHO LATER DIED OF CANCER—ANALYSED BY STAGE OF DISEASE. PRIMARY OPERABLE CASES TREATED BY RADICAL

| | Admitted 1940-1942 | | Admitted 1935-1939 | | Admitted 1932-1933. | |
|---|---|---|---|---|---|---|
| Total Cases Free of Disease at five years | Breast only Involved 287 | Breast and Axilla 228 | Breast only Involved 260 | Breast and Axilla 178 | Breast only Involved 40 | Breast and Axilla 29 |
| Percentage of cases free of disease at five years who later died of cancer .. .. | — | 5.3 | 9.2. | 14.0 | 10.0 | 24.1 |

In order to compare some earlier groups of cases we took the operable cases of 1932 and 1933 who had radical mastectomies. We found that the

greater the number of years after the radical, the higher the sum percentage of recurrences. Table II reveals that those having axillary involvement are much more apt to have a late metastasis or recurrence than those having their disease confined to the breast at the time of operation.

It would appear that those operable cases having disease confined to the breast receiving an immediate radical, fared better than those who were given pre-operative irradiation. (See Table III.)

TABLE III

| Determinate Results | Admitted 1940-1942 | Admitted 1935-1939 | Admitted 1932-1933 |
|---|---|---|---|
| Primary operable cases treated with radical; breast alone involved .. .. .. | 370 | 367 | 58 |
| Percentage surviving five years .. .. | 82.2 | 74.9 | 75.9 |
| Primary operable cases treated with radical; breast and axilla involved .. .. .. | 625 | 548 | 124 |
| Percentage surviving five years .. .. | 43.5 | 40.7 | 31.5 |
| Primary operable cases treated with radical; breast alone involved.. .. .. .. | — | — | — |
| Percentage free of disease at five years .. | 77.6 | 70.8 | 69.0 |
| Primary operable cases treated with radical; breast and axilla involved .. .. .. | — | — | — |
| Percentage free of disease at five years .. | 36.5 | 32.5 | 23.4 |

## SIZE OF THE CANCER

The ultimate results of therapy are based on several variable factors, namely, the degree of malignancy, the age of the patient, the richness of the soil, the size of the tumour. In a study of the effect of tumour size on the result of treatment by radical mastectomy during the years 1935 to 1942, we found that the smaller the tumour, the greater the percentage of five-year survivals. In a small series of 22 cases with a diameter of 1 cm. or less, the survival rate was 93 per cent. (See Table IV.)

TABLE IV

FIVE-YEAR SURVIVAL ACCORDING TO TUMOUR SIZE

| Largest diameter of primary tumour | Total cases | Breast only involved | Breast and Axilla involved |
|---|---|---|---|
| Less than 2 cm. .. .. .. .. | 201 | 121 | 80 |
| Percentage surviving five years .. .. | 78.1 | 90.9 | 58.8 |
| 2.0 to 2.9 cm. .. .. .. .. .. | 397 | 185 | 211 |
| Percentage surviving five years .. .. | 67.3 | 78.9 | 56.9 |
| 3.0 to 3.9 cm. .. .. .. .. .. | 316 | 117 | 199 |
| Percentage surviving five years .. .. | 54.7 | 72.6 | 44.2 |
| 4.0 to 4.9 cm. .. .. .. .. .. | 183 | 65 | 118 |
| Percentage surviving five years .. .. | 51.9 | 67.6 | 43.2 |

## AXILLARY NODE INVOLVEMENT

In a study of node level involvement in primary operable cases treated by radical mastectomy we find the following:

| | Level I | Level II | Level III |
|---|---|---|---|
| Five-year survivals .. .. .. .. | 65.2% | 44.9% | 28.4% |

Our survival rate for those 279 determinate cases having disease confined to the breast, is 83·2 per cent. Four hundred and fifty-one cases with axillary involvement were tagged with an aluminium tag at the base, the mid-portion, and the apex of the axilla representing levels I, II, and III. The five-year survivals in this group were 44·3 per cent.

## LYMPHŒDEMA

Next to effecting a cure in breast cancer the greatest surgical problem involved in this field is lymphœdema of the arm. Owing to the importance of avoiding the condition, it might be profitable to briefly consider the causes of lymphœdema. They are the following:

1. Massive bacterial infection of the axilla.
2. Primary and metastatic disease in the axilla.
3. Obesity.
4. Heavy X-ray therapy of the axilla.
5. Lack of thorough post-operative drainage of the axilla, resulting in lymphangitis.
6. Filariasis.
7. Surgical operation with perfect wound healing; exact cause of lymphœdema unknown.

Discussion here will be limited to lymphœdema in relation to breast cancer. Lymphœdema which is due to metastatic disease is permanent and irreparable.

In our opinion all patients who have had a proper radical mastectomy, have an arm which is slightly larger than the opposite arm. During the course of the radical removal of all lymphatic chains, small veins, and axillary fat, it is to be anticipated that there will be a minimal impairment of the return lymphatic and venous circulation. This is due not only to the removal of many channels of egress from the arm, but also because there will be laid down as a part of the repair process, extra scar tissue which helps to obstruct fluid return and which lessens the calibre of vein and lymphatic channels of the local region.

I wish to emphasise that the post-operative care of the wound of a patient who has had a radical mastectomy is of importance equal to the care with which the axillary dissection is carried out. The surgeon in charge should not leave the responsibility of the surgical dressings entirely to the young assistant. As the responsibility is too great, someone of experience, who is keen in detecting small fluid accumulations, should not only carefully investigate the wound, but should inspect the wound within the proper post-operative period, namely, the third or fourth day, or *before* the time that the glazed appearance of the granulation tissue forms, which accompanies fluid collection.

If effective axillary drainage is instituted early, following the radical, there will be little opportunity for massive lymphœdema of the arm, unless the case was on the borderline of operability. However, if neglect of a sizeable axillary accumulation continues for a period of four or five days, the chances are that permanent lymphœdema will be produced. The greatest preventive measure of lymphœdema is meticulous care of the post-operative wound.

The immediate effects of heavy X-ray therapy to the axilla is an inflammatory reaction of the skin of the axilla, upper arm, and supraclavicular areas, which will impair superficial lymphatic return. The late effects of such irradiation therapy is the laying down of an additional amount of fibrous tissue which further produces lymphœdema. There is an amount of X-ray therapy over the axilla past which we should not go. Unfortunately, we dare not use a cancericidal dose of X-ray in the axilla without, in most instances, producing a lymphœdema.

The life of a patient with a lymphœdematous arm is miserable; her future is progressively worse. Not only is the weight of the arm heavy, but it feels to the patient as if it would burst. Discomfort is continuous. Localized infection and cellulitis are common. Unfortunately, there is little relief available for these sufferers. Any measure which can be employed to prevent this condition should be faithfully resorted to. In my hands the Handley lymphangioplasty has been a disappointing procedure, as has also the Kondoleon operation. As lymphœdema increases, so does the incidence of arm infection. The Kondoleon operation has contributed but little to the improvement in the size of the arm; but in large arms accompanied by frequent infections, the procedure has proved

to be of real value in reducing the number of acute attacks of cellulitis and arm infection; in some instances the infections have been stopped altogether.

The procedures of Reinhoff, and of Hutchins, in the transplantation of the latissimus dorsi muscle have, like other procedures for the relief of this condition, proven disappointing. The Treves procedure of detaching the teres major muscle from the humerus and attaching it to the under surface of the remaining portion of the pectoralis major muscle is still to be evaluated.

As cancer of the breast is the most common type of cancer attacking women, there are, therefore, an enormous number of cases of lymphœdema. There is no field of breast surgery more worthy of research than the alleviation of relief from lymphœdema.

## SKIN GRAFT

The controversy as to the necessity of a skin graft in every radical mastectomy is still going on in the United States. I feel that in the majority of cases a skin graft is not necessary. Nowadays patients come with smaller tumours than previously, giving us the opportunity to make the incision a good distance from the tumour and still get a primary closure. However, in certain instances, particularly in the upper inner quadrant, skin graft often becomes necessary.

On the other hand, some surgeons skin graft every radical. This view point we oppose as unnecessary. Furthermore, those advocates have to date been unable to prove that by skin graft they obtain a lesser number of skin recurrences than those who do not carry it out as a routine.

White has recently studied local recurrence in three hospitals, comparing those who had a plastic closure with those who had a skin graft. The results were as follows:

| *Local Recurrence* | *Five-year Results* | |
|---|---|---|
| | *Disease limited to breast* | |
| Roosevelt Hospital | Plastic .. | 10.8% |
| Presbyterian Hospital | Graft .. | 9.7% |
| Henry Ford Hospital | Plastic .. | 5.5% |
| | Graft .. | 8.3% |

We believe that the best method of avoiding a local recurrence is to leave a generous margin on all sides of the tumour, cut very thin flaps according to Handley's principles, and make a skin graft only if necessary.

The use of the opposite breast for purposes of facilitating closure has never been developed to the point that it should be used. Its use will frequently aid in making a closure that would otherwise require a graft.

### Post-operative Deaths

By a post-operative death, we mean that the patient on whom we have performed radical mastectomy does not leave the hospital alive. The

number of post-operative deaths from the radical mastectomy have greatly improved during the last 10 years. The report of Lewis and Reinhoff from Johns Hopkins Hospital, the home of the radical mastectomy, was 5 per cent., i.e., one death in 20 cases. The Henry Ford Hospital reported 4 per cent., i.e., one in 25 cases. The Presbyterian Hospital, 3 per cent., i.e., one death in each 33 cases.

Between the years 1935 to 1940 during the pre-operative irradiation years we had several deaths from infection. The post-operative wounds of those who received pre-operative irradiation followed by the radical, were very poor. The healing qualities of the normal skin flaps were greatly impaired by radiation. As we increased the amount of radiation, the quality of healing deteriorated. Following this five-year experience, we did the immediate radical mastectomy and followed the cases with post-operative irradiation over the axilla, supra-clavicular and infra-clavicular areas, if the axilla were involved. From the start of this regime to the present, our operative mortality has decreased to 0.3 per cent., or one death in each 325 cases. These deaths have been chiefly cerebral accidents in women with blood pressure of over 230, or cases of coronary thrombosis, or pulmonary embolus.

During the nine-year period of 1939 to 1948, 4,544 radical mastectomies were performed. The 14 operative deaths were due to the following causes:

| | |
|---|---|
| Pulmonary Embolus .. .. .. .. .. | 5 cases |
| Cerebral accident .. .. .. .. .. | 4 cases |
| Coronary or Cardiac .. .. .. .. .. | 3 cases |
| Shock .. .. .. .. .. .. .. | 1 case |
| Uncontrolled Diabetes .. .. .. .. .. | 1 case |
| Infection .. .. .. .. .. .. .. | 0 |

The above list shows that infections which were the chief cause of post-operative death during the preceding five years completely disappeared from our causes of death.

## PAPILLOMATOSIS

Sanguinous or sero sanguinous discharge from the nipple is indicative of the presence of a papilloma, or papillary cyst adenoma or carcinoma. It has been the teaching of the past that a papilloma should be removed because it frequently develops into carcinoma. It is the practice of surgeons to remove the papilloma locally or perform a simple mastectomy, if they could not palpate the lesion. If the lesion appears to have the characteristics of a pre-cancerous papilloma surgeons usually do a simple mastectomy.

About eight years ago we raised the question as to how the pathologist could unequivocally predict that what he thought to be a pre-cancerous papilloma would actually continue along the line indicated by the ominous appearance and actually develop into cancer. We thought it

would be worth while to test out the established viewpoint. Consequently, we ceased performing a simple mastectomy on even those cases with the direst reports of the pre-cancerous state, and even those cases with reports warning us that this was a lesion which appeared particularly apt to develop into cancer. We fully recognised our responsibility and at first were often worried over our position. However, we are happy to report that as far as we know, not one case of papillomatosis has developed a cancer to date. During these eight years there have been approximately 416 cases of papillomatosis, many of which had developed marked pre-cancerous appearance. The fact that none of these cases has developed cancer makes one recognize that (*a*) papillomatosis is not a pre-cancerous lesion, (*b*) that the appearance of pre-cancerous attributes in the papilloma is a false appearance and (*c*) that the generally accepted and well established viewpoint concerning the development of papillomas into cancer is false. These are bold statements, but I am sure that as a rule they are true.

We then come to the next viewpoint, that the papilloma is a benign lesion and remains benign ; and those cases of bleeding nipple with cancer as the cause of the bleeding, began as carcinoma—and did not develop from a previously benign papilloma. There are pathologists who state that they can trace the steps resulting in carcinoma from a papilloma, but we must disagree with their deductions and conclusions from their evidence.

In my experience the majority of papillomas are situated close to the nipple, within or at the edge of the areola, while the carcinomata which produce bloody discharge are apt to be located further out in the mid zone.

From this viewpoint it is obvious that much mutilating surgery will be unnecessary.

## CYSTS

There is an enormous amount of confusion as to what procedure is best in cases of cysts, cystic disease and cystic mastitis. These three terms for practical purposes may be used synonymously. World literature on the subject is conflicting, leaving the reader in a quandary as to whether cystic disease is pre-cancerous, and if so what should be the surgical procedure indicated. One school of thought says that cystic disease represents a pre-cancerous state. Among other proofs of evidence Shields Warren of Harvard proves his contention that these conditions are pre-cancerous by statistical studies of cystic mastitis when compared with the general population of Toronto and Boston.

Our personal viewpoint is quite the contrary. We do not believe that cysts, cystic mastitis and cystic disease are pre-cancerous lesions. In fact, if cancer subsequently develops in a breast following the removal of a cyst or area of cystic mastitis, it does not occur in the cyst wall, but it develops in the interstitial tissue, between the multiple cysts.

We feel that this condition represents a hormone deficiency disease, probably ovarian in origin. It not infrequently occurs that breast cysts develop within a month or two following the removal of the ovaries.

The average age at which cysts most frequently develop is 44 years. The average age of menopause in New York City is 46½ years. The life history of cystic disease is represented first by microscopic cysts, and dilatations along the ducts. This picture is seen usually from about 35 to 40 years of age. From then on we may find cysts of varying sizes which may have become large enough to come into the field of clinical observation. At this time one may literally find hundreds of tiny miniature blue cysts, 1 or 2 mm. in diameter. As ovarian function decreases, cystic disease increases. It is my belief that cysts and cystic disease are so common in females that the condition is not far from normal for one who is approaching her menopause. In those women who develop multiple cysts, they as a rule continue to develop cysts up and until the actual menopause. With the complete cessation of menstrual periods, the cysts spontaneously disappear, and do not return. It is most unusual for a single cyst to develop in the twenties or early thirties, or past 60 years of age. If one does, there is something unusual in the output of the ovarian hormones. As this disease is self limiting, has a normal period of development, and spontaneously disappears with the menopause, the attitude of the surgeon toward the problem should be along the line of understanding its life history. It is obvious that if a cyst appears, his first obligation to the patient is to make the diagnosis definite. This he may do in two ways. If the cyst is large, it is usually an easy matter to aspirate the cyst. If the fluid is clear, amber or cloudy, one is dealing with a simple cyst. If the cyst be deep in the breast, is only approximately 1 to 1.5 cm. in diameter, it often becomes necessary to locally remove the lesion to definitely establish the diagonosis. At this size, the lesion is hard and fluctuation cannot be elicited. We strongly oppose the idea of a simple mastectomy for cystic disease. In my opinion there is no place where more unnecessary surgery is done than in cystic disease.

Having established the diagnosis, and remembering that it is usually a bilateral disease, our habit is then to check the condition of the breast periodically, at six-month intervals, until the arrival of the menopause. We do not keep on operating on every new cyst that develops. Following the establishment of the diagnosis, more cysts as a rule develop from time to time. If the patient is in the age between 37 and her menopause; if she has a rounded tumour which is slightly tender to palpation; and if the tumour is free from any of the classic signs of cancer, we keep checking that case, rather than repeat the operation. In an experience of approximately 400 cyst cases, I have only had to operate for subsequent breast cancer three times. Keeping this group of cases under observation two or three times a year, we are able to keep a check on their condition and pick up any carcinoma in an early stage if one develops.

## IMPROVEMENT IN RESULTS

During the past 15 years there have been definite improvements in results of therapy of operable cases of breast cancer who received radical mastectomy. This is brought out by the following:

FIVE-YEAR SURVIVALS IN CASES TREATED BY RADICAL MASTECTOMY

| | 1940-1942 | 1932-1933 |
|---|---|---|
| Breast alone involved .. .. | 82.2% | 77.6% |
| Breast and Axilla involved .. | 43.5% | 31.5% |

As would be anticipated there is not much improvement in those operable cases treated by radical mastectomy when the disease is confined to the breast—only 6 per cent. On the other hand there is great encouragement for us in those cases where the disease involves both breast and axilla; here the improvement reaches the astonishing figure of 38 per cent.

There are two ways to explain this improvement. In the first place we believe that volume of surgical experience counts for something. For the past few years over 600 radical mastectomies are performed each year on my service; and I personally do 250 a year. When my own results are compared with those of my house officers and assistants, we find in those cases having axillary involvement that my percentage of five-year survivals is 4 per cent. better than theirs. This signifies that one more case in every 25 of those with axillary involvement operated on by one with greater experience, will survive the five-year period than those done by the younger, less experienced house officers who are learning how to perform the operation. Careful handling of cancer material during the course of the axillary dissection is of greatest importance. It is even probable that some cases with voluminous axillary involvement are made worse by the operation. We find it human and almost universal that a young surgeon has a strong urge to touch the node involved with cancer, either with hand or instrument. As the axillary areolar tissue is being brought down from above the level of the axillary and subclavian veins, and from over the brachial plexus, it should be covered with gauze pads to keep the operator's glove from touching diseased tissue, thereby minimising any dissemination. This may all seem too trivial to speak of, but such points obviously are what should be emphasised and never are.

The second, and probably the most important cause for improvement in results of therapy, is the fact that our patients come earlier to surgeons than formerly. This is not to be proven by the percentage of operable cases coming with involved axillæ. In fact we are disappointed to realise that our operable material still comes with 60 to 62 per cent. having axillary involvement. However, the important improvement shows itself in the volume of disease found in the axilla at operation. Less and less cases come with bulky axillary disease.

In closing we wish to state that advocates of radical surgery have waited long and impatiently for improvements to take place. However, there are signs on every hand of improvement.

In mammary cancer, the sparks fly wide, and it is still one of our most dreaded types of cancer. On the other hand, it is one of our most curable. We believe that constant improvement in the results of therapy are taking place and can further take place in the operable cases, due to greater skill in surgery and to the earlier appearance of the patients.

Probably one of our greatest reasons for encouragement in breast cancer is just being developed in the hormone field. We now know that certain chemicals have the power to heal the ulcers of breast cancer, to fill in areas of destroyed bone, to relieve pain and disability, to overcome the anæmia of cachexia by doubling the amount of hæmoglobin; and the hormone can even give a sense of well being. Any chemical agent which can perform such a miracle should be speedily and urgently investigated by teams of chemists, biologists and clinicians. There are now 600 chemicals whose value remains to be studied. The next 10 years of hormone investigation may well prove to be the most important decade since the introduction of the radical mastectomy.

## SAYINGS OF THE GREAT

"Knowledge advances by steps and not by leaps."—*Macaulay.* (Contributed by H. L. M. Roualle, F.R.C.S.)

"A surgeon must be a physician first and last; otherwise he is little more than a muddler; an amateur mechanic—and often a poor one at that."—*Sir William Macewen.* (Contributed by C. Allan Birch, F.R.C.P.)

"He is the best doctor who knows the worthlesness of most medicines." —*Benjamin Franklin.* (Contributed by C. Allan Birch, F.R.C.P.)

"Never believe what a patient tells you his doctor has said."—*Osler.* (Contributed by C. Allan Birch, F.R.C.P.)

*Note.*—Contributions are invited.

## THE RESTORATION AND DEVELOPMENT FUND

AMONG THE MEMBERS of 20 years' standing elected to the Fellowship of the College was Mr. Arthur Wai-tak Woo, in recognition of his distinguished surgical work and the high professional and academic position he holds in Hong Kong. On receiving the intimation of the distinction Mr. Woo took the next plane to England to attend the Council meeting and to be admitted. Before his return by the first plane after the meeting he made a donation of one hundred guineas to the Restoration and Development Fund. This evidence of his allegiance to the College and his appreciation of the honour conferred on him is highly valued by the Council.

# MALIGNANT DISEASE OF THE MOUTH

Lecture delivered at the Royal College of Surgeons of England
on
9th September, 1948
by

Sir Stanford Cade, K.B.E., C.B., F.R.C.S.
Surgeon, Westminster Hospital

MALIGNANT TUMOURS of the mouth are lesions of the mucous membrane, epithelial in origin and of well-defined histological character. Such lesions occur in any part of the mouth, but their progress and development vary with the actual site ; thus the natural history of a lesion of the tongue differs a little from that of a lesion of the gum or of the palate and the treatment of each anatomical site requires different operative procedures and various radiation techniques.

Radiotherapy to-day holds first place in the treatment of the primary growth. Surgery remains the method of choice in the eradication of cervical lymphnodes providing they are operable, and in the treatment of the primary lesion in certain sites such as the palate, the mandible and sometimes the tongue itself.

## THE NATURAL HISTORY OF ORAL CANCER

It is not a common disease and accounts for only 3 per cent. of cancer deaths, that is about 2,000 cases a year in England and Wales. It is nearly four times more common in men than in women. It is often preceded by degenerative changes described as " precancerous " ; these include the leukoplakias, the atrophic changes associated with Plummer-Vinson's syndrome, avitaminosis, specially of the vitamin B complex, and rarer to-day, but more common in days gone by, syphilitic glossitis. Oral sepsis of the gross variety, where the teeth are covered with tartar, the gums receded and spongy, are not infrequently found in cases of oral cancer and occasionally a simple traumatic (dental) ulcer undergoes malignant metaplasia. It is also noted that chronic alcoholics provide more than their statistical share of the total of cancer of the mouth. Tobacco by itself appears to have no carcinogenic effect ; but the heat of the smoke, the well-known " smokers patch " cannot be ruled out as a precipitating factor in the initiation of a lesion.

## MORBID ANATOMY AND HISTOLOGY

Like all epithelial cancers, those in the mouth occur in three gross anatomical varieties—the wart, the ulcer, the node ; hence the clinical varieties of papillary, ulcerative and nodular lesions. The interest to the clinician is the variation in the degree of malignancy ; the worse being the nodular infiltrating type, whilst the most amenable to treatment is the papillary or warty growth. The ulcerative type, intermediate in degree

of malignancy is the most common in the mouth as a whole, but not in the tongue, where the papillary group predominates. Like most tumours the histological study shows degrees of differentiation and the well-known Broders' classification applies here. Keratinization or formation of cell nests, mature epithelial cells and embryonal or anaplastic cells predominate in greater or lesser degree. The importance of histological varieties lies chiefly in their relationship to early lymphnode invasion. The greater the anaplasia, the sooner the lymphnodes are invaded. The most malignant types are also the most sensitive to radiation. It must be remembered that radio-sensitivity does not mean radio-curability, and the lesions which melt quickly are as a rule the most lethal. Besides the four grades, according to Broders, a rarer variety, the " lympho-epithelioma " has drawn attention since its first description in 1921. This type, where anaplastic, round, pale-staining cells are found in close association with small dark-staining lymphocyte-like cells, occurs in the upper air passages and air sinuses, as well as in the mouth. It is a highly radio-sensitive tumour which occurs more frequently in the posterior or pharyngeal part of the tongue and gives rise to large widespread lymphnode invasion. Some authorities have recently reverted to the view that these lesions are a type of reticulum cell sarcoma and their high degree of radio-sensitivity supports this view.

## INCIDENCE

There is a definite decline in the incidence of cancer of the mouth, chiefly of the tongue itself. This decrease however applies to men only.

Table I shows the trend of incidence in the recent 10-year period.

TABLE I

INCIDENCE OF CANCER OF THE MOUTH AND TONGUE

Mortality in England and Wales

| Year | Mouth and Pharynx | | Tongue | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| 1937 | 2,639 | 562 | 926 | 130 |
| 1938 | 2,591 | 566 | 884 | 129 |
| 1939 | 2,432 | 561 | 812 | 122 |
| 1940 | 2,451 | 548 | 863 | 139 |
| 1941 | 2,298 | 525 | 764 | 137 |
| 1942 | 2,261 | 514 | 779 | 139 |
| 1943 | 2,186 | 548 | 734 | 166 |
| 1944 | 2,153 | 536 | 756 | 156 |
| 1945 | 2,003 | 526 | 656 | 146 |
| 1946 | 1,869 | 527 | 602 | 123 |

The curability rate by modern methods of treatment, although better than in pre-radiation days, remains low. In early cases, in the best centres 55 per cent. of 5 year survival with freedom of disease is recorded; in late cases, only 10 per cent. survive 5 years and all groups together show about 25 per cent. of 5 year survival. Here, as elsewhere, early diagnosis is of primary importance; equally so is a sound selection of the method of treatment and a technique of high order, both surgical and radiological is essential, if regression of the lesion is to be obtained.

## SIGNS AND SYMPTOMS

The manifestations of the disease in its initial stages are slight. Discomfort and the sensation of a "lump" felt either in the tongue or by the tongue, in the floor of the mouth, the cheek or the gums are the most common early symptoms. Discomfort may be present on eating, or in the case of the posterior part of the mouth (fauces, pharyngeal aspect of the tongue and the soft palate), on swallowing only. Pain is a late symptom, so is increased salivation and hæmorrhage and blurring of speech. On examination in a good light, the whole mouth must be carefully inspected and the use of a laryngeal mirror is essential as otherwise quite extensive lesions may be missed. The lesion itself—whether it be an ulcer or a warty growth—is characteristic to the initiated; to the mind of the non-initiated the possibility of a neoplasm as the common *persistent localised* lesion should be ever-present. The most common mistake is to suspect the lesion to be syphilitic, and no greater misfortune can befall a patient, the bearer of a positive Wasserman, than that his past misfortunes should be taken as an explanation of the oral lesion. Tertiary Syphilis of the mouth is rare and responds rapidly to treatment. Syphilitic glossitis is a predisposing factor of oral cancer and not an indication that the lesion is benign. Nevertheless, bacteriological and serological examinations should be done rapidly and if doubt still exists a biopsy must be performed. The biopsy must be taken from the margin of the lesion, should include apparently normal tissue and be of sufficient depth; as a rule a cube of tissue half a centimetre in depth is adequate. The presence of enlarged lymph glands, their size, their site and their consistency, should be ascertained by palpation. Some glands when enlarged are inflammatory only; others, even when not palpable, may be the seat of metastases. Gross enlargement of one group of glands and fixation to the main vascular bundle are evidence of advanced disease; such glands may be present when the primary lesion is still small and clinically favourable. Superadded infection may produce rapid enlargement of a gland with a small metastasis in it. Bilateral glands occur frequently in the case of lesions of the soft palate and when the whole tongue is involved; contra-lateral enlargement is occasionally seen in a strictly unilateral lesion.

## DIAGNOSIS

The examination of the patient should be directed to the establishment of a diagnosis, not only of the nature of the disease, but of its exact

origin, its extent, the involvement of adjoining tissues and the presence of lymphnode metastasis. It must be emphasised that a good deal of time is often lost before a diagnosis is established; the delay in most cases is due to lack of appreciation that the most common persistent lesion of the tongue is a cancer and that a positive Wasserman test does not exclude it. Benign and inflammatory lesions can mimic cancer but the reverse is not true. Biopsy if adequate establishes the diagnosis and should not be delayed.

## PROGNOSIS

The curability rate of carcinoma of the buccal cavity depends, as in other sites, primarily on the extent of the lesion, but in addition, the actual site of the disease profoundly affects the prognosis. In importance, the two factors *extent* and *site* can be bracketed as equal. Histological classification and degree of malignancy are of far lesser prognostic significance. Extent of the disease can best be studied in relation to site and the main classification is therefore anatomical. In addition, the presence or absence of lymphnode invasion divides all cases into two main groups—with or without metastases. I will pass briefly in review the five common sites: (1) Tongue; (2) buccal mucosa; (3) alveolar mucosa; (4) the palate and (5) the floor of the mouth. In all lesions it must be emphasised that dental caries, pyorrhœa and the very presence of teeth even apparently healthy, complicates treatment and lowers the curability rate. It is well known that an edentulous mouth is the greatest asset to any form of treatment, surgical or radiological.

*Tongue.*—This study is based on 365 cases of cancer of the tongue in a series of a total of 550 cases of malignant lesions of the mouth. It covers a period of 25 years. It includes the 1939-45 period when I was absent on war service and this period has considerably affected the follow-up of cases and the statistical survey of results. It is computed that in England and Wales, 1,000 persons die every year from cancer of the tongue. On the presumption that for every death there are three cases alive with the disease, this brings the total incidence only to 75 cases of cancer of the tongue per million people living. It is therefore necessary to concentrate these patients in as few centres as possible, or the individual experience of the surgeon or radiotherapist becomes negligible.

## CHOICE OF METHOD OF TREATMENT

The treatment of choice is radium; in about 7 per cent. of cases, surgical excision is indicated and this small group includes the following: (1) where the disease has transgressed the floor of the mouth and involved the mandible; (2) where the entire tongue is involved in its anterior part down to the V of the circumvallate papillæ by a hard infiltrating growth; (3) in cases which have failed to respond to radiation, either as an immediate failure with but slight regression of the lesion or when recurrence of active disease takes place within a few months of treatment. If surgery is decided on, ablation of the requisite part of the tongue and

adjoining tissue is preferably done by diathermy; if the alveolus is involved, part of the mandible is resected.

*Radium Therapy.*—For lesions of the anterior part of the tongue insertion of radium needles is the method of choice. In lesions of the valleculla, epiglottis, glosso-palatine folds, or in the posterolateral group spreading to the alveolar mucosa or palate, teleradium is used. X-ray therapy as the sole method of treatment in cancer of the tongue is disappointing, although as an additional source of radiation in cases treated by teleradium, it has proved useful. In both types of cases and in superficial lesions of the floor of the mouth or palate intra-oral plaques (moulds) are occasionally used to supplement needling or teleradium; especially in cases where, at the junction of the tongue and upper or lower alveolus or the palate, uniform distribution or radiation and an adequate dose are difficult or impossible to achieve by other means.

*Distribution or Radiation and Dosage.*—To obtain a homogeneous distribution or radiation in the lesion and surrounding tissue, to assess the quantity of radium needed, and to determine the dose from a given arrangement of needles, the co-operation of a clinically trained physicist is a primary essential. The actual insertion of needles or seeds and their retention in the tissues for the desired time require a certain degree of surgical skill. The lesion in the tongue is carefully examined and its extent, position, shape and volume ascertained. The spatial distribution of the needles must fulfil certain physical conditions and the dosage system devised by Paterson and Parker, first for surface application and subsequently for interstitial therapy, remains the simplest, the most useful and generally accepted method. The total dose has varied from 6,000r. to 10,000r. delivered in 168 hours; the dosage rate showed an equally wide range from 30 to 75r/hr. For interstitial treatment an average of seven days is used.

*Teleradium.*—A vast amount of clinical, physical and biological research has been done in the past 15 years. The magnitude of the task can be illustrated by the problems which the treatment presents: total dose, dosage rate, time of individual treatment, interval between treatments, overall time of treatment. From the physicist's point of view in the use of beam therapy—the direction of the beam, the combination of multiple ports of entry, and the spatial distribution of radiation are some of the problems. Limitations imposed by the maximum tolerance of the skin, the anatomical configuration of the part traversed by the beam, and the position of the lesion are so many added difficulties. To overcome these practical difficulties and to ensure an optimum arrangement for the fields in each individual case, H. T. Flint and C. W. Wilson have constructed suitable frameworks or "jigs" for the various parts of the neck which provide the position of the fields and the direction of the beam. Wilson has thus contributed the principle and provided the

facilities for placing the patient within a known field of radiation in preference to providing unknown fields within the patient.

Using the present model of the 10 gramme radium unit at Westminster Hospital it takes three to four weeks to treat a lesion in the pharyngeal portion of the tongue; two or three treatments of 20 minutes each are given daily five days a week. The average tissue dosage is between 6,000—7,500; the skin reactions are less severe with the 10 gramme unit than with smaller units used previously.

## TREATMENT OF CERVICAL LYMPHNODES

The wide dissection or " block " dissection associated with the names of Butlin, Crile and later, Roux-Berger remains the most certain method of treatment.

The operation consists in the removal of the deep cervical fascia from the level of the mandible to the clavicle; the sternomastoid muscle, the internal jugular vein, the anterior belly of the omohyoid and often the posterior belly of the digastric are removed, together with the glands in the anterior and submaxillary triangles. The indications for this operation are quite clear cut: (1) The primary lesion in the tongue should be healed and there must be a reasonable prospect of permanent regression. (2) The glands although palpable and clinically malignant should be mobile or only slightly adherent; they must be not only " removable " but strictly operable. (3) The general health of the patient should not be such as to preclude a major operation. It is necessary to emphasise that the operation should not be undertaken unless these conditions prevail. Incomplete removal is doomed to failure and is invariably followed by local recurrence.

If a block dissection is deemed unsuitable, irradiation by teleradium and X-rays is the second-best available. There is, however, a group of cases where interstitial radiation is indicated; when the lymphnodes are matted together and form a hard fixed mass, a two-plane or volume implant can be carried out. Long radium needles of low intensity, that is 2 or 3 mg. of radium in an overall length of 6 cm. are inserted into the mass and left in situ for seven days. The dose aimed at is 8,000r. Shrinking of the mass and arrest of the disease for one to two years can thus be achieved.

## RESULTS

The results obtained in the series of cases are indicated in the following tables:

TABLE II

CANCER OF THE TONGUE

| | |
|---|---|
| Total number of cases .. .. .. .. .. | 365 |
| Indeterminate group .. .. .. .. .. | 50 |
| Determinate group .. .. .. .. .. | 315 |

TABLE III
CANCER OF THE TONGUE
DETERMINATE GROUP

| | |
|---|---|
| Dead from Cancer .. .. .. .. .. | 209 |
| Dead from other causes (Cancer present) .. .. | 25 |
| Lost trace of (probably dead) .. .. .. .. | 32 |
| Total number of failures .. .. .. .. .. | 266 |
| Free from disease .. .. .. .. .. .. | 99 |

Percentage of 5-15 years survival: 27 per cent. all cases, 31 per cent. determinate.

TABLE IV
CARCINOMA OF TONGUE, 1924-1939

| | Total | Alive: 5 years free of disease | Per cent. |
|---|---|---|---|
| | 220 | 49 | 22·3 |
| Anterior .. .. | 24 | 5 | 20·8 |
| Posterior .. .. | 89 | 16 | 17·9 |
| Inferior .. .. | 37 | 8 | 21·6 |
| Lateral .. .. | 70 | 20 | 28·6 |

TABLE V
CARCINOMA OF TONGUE, 1924-1939
RESULTS IN VARIOUS STAGES

| | Total | Alive: 5 years free of disease | Per cent. |
|---|---|---|---|
| | 220 | 49 | 22·3 |
| Early Cases .. .. | 30 | 17 | 56·6 |
| Without Glands .. | 60 | 20 | 33·3 |
| With Glands .. .. | 130 | 12 | 9·2 |

## CANCER OF THE TONGUE: SUMMARY

(1) The method of treatment is radium needling to the tongue in anterior lesions and Teleradium in posterior lesions.

(2) Exceptions are:
   (*a*) When the lesion involves the mandible.
   (*b*) When the whole tongue is involved.
   (*c*) When previous radium has failed to cure the lesion. Such cases are treated by surgical excision.

(3) Cervical lymphnodes are treated by:
- (*a*) Block dissection of the neck.
  - (i) When the primary lesion is soundly healed.
  - (ii) When the lymphnodes are enlarged and strictly operable.
  - (iii) When the age and general health of the patient permit a major surgical procedure.
- (*b*) By teleradium:
  - (i) When the primary lesion has not entirely regressed.
  - (ii) When the lymphnodes are not strictly operable—adherent to deep fascia, etc.
  - (iii) When the general health does not permit a major procedure.
- (*c*) By interstitial radium:
  When there is a fixed mass of lymphnodes.

## BUCCAL MUCOSA

Carcinoma of the buccal mucosa accounts for about 10 per cent. of all intraoral neoplasms. It is a disease of the elderly and old patients and occurs mostly in men (80 per cent.). There is a close relationship to precancerous conditions, such as leukoplakia, chronic irritation from sharp carious teeth, tobacco chewing and indeed where betel-nut chewing is common, cancer of the cheek accounts for about one-third of all oral neoplasms. As compared to other sites in the mouth, it is the most favourable site. Metastases are present in about 40 per cent. of cases. Metastases occur more frequently when the lesion extends beyond the cheek to the gingival sulcus, the faucial pillars and in cases where unsuccessful attempts at local treatment by ineffectual means are tried before the patient is referred to hospital. In this connection, it is important to remind both doctors and dentists that repeated local application of silver nitrate seems to be a very effective way to precipitate the development of oral cancer.

*Treatment.*—The buccal mucosa has proved a most suitable site for radiation therapy, which has in fact entirely replaced surgical excision in centres where facilities for adequate radiation are available. That this is in fact the method of choice is shown by the high five-year survival rate with freedom of disease—61 per cent. in my own series. Permanency of regression can be confidently anticipated and a number of 15 to 18 year survivals are on record. It has been my experience that radium is more effective than X-ray therapy at 200 K.V. The lesion of the buccal mucosa can be treated with ease by teleradium, intra-oral mould or radium implant. I prefer interstitial radium by a single plane implant delivering a minimum of 8,000r. in seven days, but frequently 10,000r. or even more is given without ill effects. With careful attention to the distribution rules, an accurate and even filming is obtained over the buccal mucosa and the lesion resolves completely in about 14 days. The dose is limited to 6,000r. only in the very old, where the tissues are frail and delicate and the reaction

apt to be severe and the risk of necrosis greater than in the average patient. This method has the advantage of accuracy and speed ; it is the method of choice for the average lesion. Intra-oral moulds are only exceptionally used and teleradium reserved only for advanced lesions where the whole thickness of the cheek is involved by the growth.

## ALVEOLAR MUCOSA

Carcinoma of the alveolar mucosa is a clinical entity. The commonest site is the posterior third of the alveolar region. It is three times more common in the lower than in the upper jaw ; in some cases both upper and lower alveoli are involved. As long as the disease is localised to the gum, lymphnode involvement is rare, but with the spread of the lesion to the adjoining part of the mouth (buccal mucosa, floor of the mouth and palate) the incidence of glandular metastasis rises sharply ; sooner or later, the adjacent bone is involved.

Unless the bone is obviously involved, radiation should be tried as the first method of treatment. If the bone is involved, surgical excision forms the main attack, but pre-operative radiation is always an advantage. In small and superficial lesions intra-oral moulds can be effectively used. In extensive lesions not involving bone, teleradium is more effective. If the upper alveolus is involved, diathermy resection of the diseased alveolus and post-operative intra-oral mould is the routine at Westminster Hospital. In the case of the lower jaw, resection is a rapid and adequate method of dealing with the lesion. There is a great variability in the radiosensitivity of carcinomata of the alveolar mucosa ; some cases regress completely with as little as 3,500r., others remain unaltered or regress only slightly with twice that dose. The response to radiation is not always dependent on the histological type of the neoplasm. The treatment should consist in every case of preliminary radiation and if total disappearance of the lesions is not obtained rapidly, say within one month, surgical excision should be carried out.

## THE PALATE

A very important clinical subdivision of cases is that of tumours of the *hard* and *soft* palate. The prognosis and many clinical features in the natural history differ so widely as to constitute two separate clinical entities. Thus the sex incidence is equal in tumours of the hard palate, whereas in the soft palate, men are affected very much more often than women. But above all, it is the glandular involvement and hence the prognosis which differs greatly. Whereas in the hard palate, 30 per cent. of cases show lymphnode metastases, the incidence in the lesions of the soft palate is twice as great, namely 60 per cent. Further, in the case of the soft palate, bilateral cervical glands are very frequently met, even in cases where the lesion is unilateral.

The primary tumour in the palate is in most cases, radiosensitive and the treatment presents no great difficulty, but if improvements in end-results are to be obtained, some re-orientation is necessary in the accepted method of treatment, specially of the lymphatic areas.

## TREATMENT OF THE PRIMARY GROWTH

The scheme of treatment depends in a great measure on the site, extent and type of lesion. The general principles of the selection of the method of treatment can be summarised as follows :

(*a*) *The hard palate.*—In early cases, intra-oral surface irradiation by means of a prosthesis is accurate, simple and effective. In extensive lesions, teleradium is the method of choice. In all cases, local diathermy excision preceded by radiation gives the advantages of both radiation and surgery, and combined radiological and surgical treatment remains so far the best method.

(*b*) *The soft palate.*—Both X-rays and teleradium have given total regression of the primary growth. Surgery by itself seems a futile procedure which, besides considerable functional disability as regards speech, only very exceptionally gives a five-year survival. Most soft palate carcinomata are radiosensitive and radiation should in all cases be the first choice. My personal experience is much greater with teleradium and this forms the main method of treatment. Surgical treatment of carcinoma of the palate, when not successful (that is in the majority of cases), seems to accelerate the development of cervical metastases.

## THE FLOOR OF THE MOUTH

Carcinoma of the floor of the mouth is recognised in its early stages only ; in extensive lesions, direct spread involves the under surface of the tongue or the gingival mucosa. Direct spread to the submental area through the extrinsic lingual muscles also occurs. Lymphnode involvement occurs in over 70 per cent. of cases ; the degree of malignancy is high, curability rate however is about 40 per cent. of five-year survival with freedom from disease in cases still localised to the floor of the mouth.

*Method of Treatment.*—Surgical excision is reserved for cases where the mandible is involved. These cases are not curable by present day methods of radiation, with the occasional exception which proves the rule.

In lesions not involving bone, but spreading to the intrinsic muscles of the tongue or to the extrinsic muscles of the floor of the mouth, interstitial radium is the choice ; in small lesions, strictly localised to the mucosa of the floor of the mouth, X-rays, seeds and teleradium have all been equally successful.

In comparing the various sites, the ends results at five years indicate the relative degree of malignancy. In my own series of cases five-year results free from disease are shown in Table VI.

TABLE VI

FIVE YEAR SURVIVAL IN VARIOUS SITES OF ORAL CANCER

| | |
|---|---|
| Soft Palate .. .. .. .. .. .. | 5 per cent |
| Hard Palate .. .. .. .. .. | 53 per cent |
| Buccal mucosa .. .. .. .. .. | 61 per cent |
| Alveolar mucosa .. .. .. .. .. | 16 per cent |
| Floor of the Mouth .. .. .. .. .. | 41 per cent |

## TREATMENT OF THE LYMPHATIC AREAS

The principles accepted in the management of the cervical glands in the case of cancer of the tongue apply to cancer of the buccal cavity in general. They can with benefit be recapitulated now. Surgery remains the method of choice. It is applicable only in strictly operable cases. It should be on a wide scale, what is known as the block dissection of the neck. It must include the deep cervical fascia from mandible to clavicle and from the midline anteriorly to the anterior border of the trapezius; it must of necessity include the sterno-mastoid muscle and the internal jugular vein and frequently the digastric and omohyoid muscle.

The procedure is no longer practised as a prophylactic measure, when no enlarged glands are palpable. It is useless if the glands are adherent. It should not be undertaken unless the primary growth is controlled and there is a reasonable chance of permanent regression. It should not be done in the old, and in patients with poor general health. With these limitations, it remains the most effective measure in the control of malignant cervical glands.

Irradiation by X-rays or radium as a prophylactic measure, that is in the absence of palpably enlarged glands is indicated only in the case of carcinoma of the soft palate In all other lesions, treatment should only be given in the presence of enlarged glands. In localised masses of glands, external radiation is the first method, if it fails, needling of the mass is of great palliative value.

## SUMMARY

As in cases of cancer of the tongue, so in lesions of the buccal cavity, radium is of considerable value either alone or in combination with surgery in selected cases. The limitations of radium are: radio-resistance of the neoplasm, inaccessibility of the lesion and limitation of the tissue tolerance, skin and mucosa. In small lesions, the optimum dose is 8,000-10,000r. X-ray therapy in buccal cancer is of limited value and the percentage of five-year cures is considerably lower than with radium.

# LIVER FUNCTION TESTS

Lecture delivered at the Royal College of Surgeons of England

on

29th November, 1948

by

L. E. Glynn, M.D., M.R.C.S., M.R.C.P.
Director of Pathology, Canadian Red Cross Memorial Hospital, Taplow

STUDY OF hepatic dysfunction is complicated by three peculiar attributes of the liver, namely, the great number and variety of functions it performs, its large functional reserve, and its extraordinary powers of regeneration after injury. Any single laboratory test devised as a means of assessing hepatic function only tests one or a group of related functions, and must not be taken as an indication of the activity of the liver with respect to other of its functions. Thus, impairment of its powers of pigment excretion does not necessarily imply any significant change in its synthetic or detoxicating powers, and vice versa. Moreover, owing to its large functional reserve, extensive liver injury may remain undetected by any of the usual function tests, and conversely a positive laboratory test for impaired function implies an extensive hepatic injury. Nevertheless such evidence of extensive injury is frequently obtained, but does not carry the same disturbing prognosis as would evidence of a similar degree of injury in any other vital organ. This is because the regenerative capacity of the liver is such that 75 per cent. of its parenchyma can be regenerated in a few weeks whether the initial deprivation be the result of surgical removal, chemical injury or vascular occlusion. This does not by any means vitiate the value of function tests in helping to assess the nature and severity of liver lesions, but it indicates their subservient place amongst the data required for the correct diagnosis in any individual.

There are at least four reasons for carrying out liver function tests. Primarily and most frequently they are used as aids in differential diagnosis. Secondly, they are of considerable use in following the course of established disease, for example, infective hepatitis or hepatic cirrhosis. Thirdly, and more rarely, tests are carried out because of interest in the function itself rather than as an indication of hepatic function in general; for example, the estimation of plasma prothrombin prior to operation as an indication of defect in the blood clotting mechanism, or in the study of certain endocrine abnormalities such as gynæcomastia and testicular atrophy which may be due to the failure of hepatic detoxication. Fourthly, to detect occult hepatic damage as occurs, for example, in thyrotoxicosis.

Before considering the individual liver function tests available, it will be useful to enumerate the known functions of the liver with the evidence that indicates the corresponding dysfunction, if any. This is presented in summarised form in the accompanying table.

## Known Liver Functions and Evidence of Corresponding Dysfunction, if any

### A.—Physiological Excretion.—Includes all known bile constituents.

| *Constituent* | *Evidence of failure to excrete* | *Function test* |
|---|---|---|
| Bile pigment | Jaundice. Acholic stools ± bile in urine | Icterus index. Van den Bergh |
| Bile salts | Vitamin K malabsorption. Hæmorrhage. Pruritus. Bradycardia. Fat absorption | Prothrombin time. Hay's Test |
| Urobilin | — | Urinary and fæcal urobilinogen |
| Cholesterol | Xanthomata (rare) | Blood cholesterol |
| Alkali phosphatase | — | Serum phosphatase |

### B.—Storage Function

| *Constituent* | *Evidence of abnormality* | *Function test* |
|---|---|---|
| Glycogen | Possibly some diabetes. von Gierke's disease with hepatomegaly | Blood sugar curve Liver biopsy |
| Hæmopoietic factor | Macrocytic anæmia | Blood examination |
| Vitamins A, B, C, D, K | Signs of avitaminosis | Response to liver extract |

### C.—Serum Protein Synthesis

| *Constituent* | *Evidence of abnormality* | *Function test* |
|---|---|---|
| Serum albumin | Œdema (rare). Ascites | Serum proteins and albumin globulin ratio |
| Globulin, especially gamma | — | Flocculation tests |
| Fibrinogen | Hæmorrhage (rare) | Plasma fibrinogen |

### D.—Intermediary Metabolism

| *Function* | *Evidence of impairment* | *Function test* |
|---|---|---|
| Galactose to Glucose | — | Oral tolerance test. Blood clearance test |
| Deamination of $NH_2$ acids | Low urinary urea and ammonia | Urinary examination |
| Cholesterol esterification | — | Plasma cholesterol partition |

### E.—Detoxication and Excretion of Foreign and other Substances

| *Function* | *Evidence of impairment* | *Function test* |
|---|---|---|
| Hippuric acid synthesis | — | Hippuric acid excretion |
| Oestrogens | Spider nævi. Palmar erythema. Gynæcomastia Menorrhagia. Testicular atrophy | Oestrogen glycuronide excretion |
| Dyes, e.g., Bromsulfalein | — | Blood clearance or biliary excretion test |

### F.—Circulatory Function

| *Function* | *Evidence of impairment* | *Function test* |
|---|---|---|
| Blood flow | Ascites. Varicosites | Blood flow by bromsulfalein excretion and arterio-hepatic vein difference |

The most frequent use of liver function tests is as an aid to differential diagnosis. The necessity for such laboratory assistance to the clinician will be emphasised by a brief consideration of the classification of liver disease from the diagnostic point of view. Liver diseases are usually diagnosed under three headings:

(*a*) Diseases which significantly impair general metabolic functions, that is *Parenchymatous Hepatitis*. This may be either primary, or secondary to circulatory impairment.

(*b*) Diseases affecting the excretory channels of the liver and only secondarily affecting parenchymal function.

(*c*) Diseases simulating hepatic diseases, for example, *Hæmolytic Icterus.*

Diseases in the first group frequently present features simulating those of the second because of disruption of minute excretory channels that may be associated with parenchymal injury, and, furthermore, diseases of the second group frequently have features simulating those of the first because of parenchymal injury resulting from the obstruction, with or without secondary infection. Herein lies the kernel of the problem of the diagnosis of hepatic disease. The importance of arriving at a correct diagnosis is emphasised by the fact that whereas diseases of the liver resulting from obstruction of the excretory channels are particularly amenable to surgical intervention, patients with parenchymatous hepatitis are particularly unsuited to such intervention and its outcome is frequently fatal.

We will now consider in greater detail the more important functional tests and the significance of their results.

## 1. THE VAN DEN BERGH REACTION

The figure gives a diagrammatic representation of the metabolism of bile pigment. This is derived entirely from the breakdown of hæmoglobin in the reticulo-endothelial system. The bilirubin thus formed is carried by the blood stream to the liver cells and here the pigment is transferred from the blood sinusoid on one side to the bile capillary on the other, whence it is carried to the interlobular bile ducts and via the hepatic ducts and common bile ducts to the alimentary canal. In the intestines, under the influence of bacterial action, the bilirubin is largely converted to urobilinogen, which is partly excreted in the fæces and partly reabsorbed in the portal blood stream and returned to the liver, from which it is re-excreted. Any urobilinogen absorbed from the intestines which escapes excretion in the liver passes to the kidneys, where it is excreted in the urine. The bile pigment produced in the reticulo-endothelial system and prior to its excretion by the liver differs conspicuously from the same pigment after hepatic excretion. The former pigment is unable to pass the renal barrier into the urine, whereas the latter penetrates readily. It also reacts less readily with the Van den Bergh colour reaction. It is therefore customary to distinguish these two types of bile pigment by the terms hæmobilirubin and cholebilirubin, respectively. This enables cases of jaundice to be subdivided into two main groups: (1) Retention jaundice in which pigment is retained within the circulation because of the inability of the liver cells to excrete it, and (2) Regurgitation jaundice in which pigment, following excretion by the liver cells, regurgitates back into the circulation because of biliary obstruction or disruption. Both the kidney as mentioned above and the Van de Bergh reaction can

distinguish between the bile pigments associated with these two types of jaundice. Cholebilirubin gives a direct reaction, whereas hæmobilirubin only gives an indirect reaction, that is, the colour only appears when the serum is pre-treated with alcohol. Several theories have been advanced to account for this difference. Pure bilirubin at pH 7.4 gives a direct Van den Bergh reaction, but added to serum gives only an indirect reaction, suggesting that the pigment is in some way combined with the serum proteins. Addition of substances that reduce surface tension, such as cholesterol and bile salts, again alters the reaction to the direct form. This suggests that the direct reaction obtained in obstructive jaundice is not due to any change in the bile pigment during hepatic excretion but due to the associated reabsorption of bile salts and cholesterol as a result of the biliary obstruction. Several alternative theories, however, have been offered to account for the difference between these two types of bile pigment. For example, hæmobilirubin is an acid with two carboxyl groups. It is insoluble in water, being held in solution in the serum by absorption on to protein. It is however soluble in alcohol and hence its ability to react with the Van den Bergh reagent in the presence of this solvent. Cholebilirubin is a neutral ammonium or sodium salt of this dicarboxylic acid, is therefore soluble in water and hence reacts with the Van den Bergh reagent in the absence of alcohol.

Since the kidney is as able as the Van den Bergh reaction to distinguish the two types of bile pigment, the principal use of the reaction is in determining whether pigments in the blood really are bile pigments or not. Since the renal threshold for cholebilirubin is approximately 2mg. per cent., the Van den Bergh reaction is of value in estimating cholebilirubin in concentrations below this level.

## 2. URINARY AND FÆCAL UROBILINOGEN

The simultaneous estimation of urobilin and urobilinogen in urine and fæces are of great value in differentiating obstructive jaundice from parenchymatous hepatitis, especially if tests are repeated at intervals of a few days. Thus the presence of urobilin in the urine excludes the possibility of complete biliary obstruction since the presence of the pigment in the urine implies the presence of bile pigment in the gut. The ability of the liver to excrete urobilinogen is one of its functions most susceptible to adverse influences and consequently the rise in urinary urobilinogen may, and frequently does, precede any demonstrable retention of bile pigment in parenchymatous hepatitis. In the retention jaundice, associated with excessive hæmolysis, extremely high figures for urinary urobilinogen are obtained partly because of the excessive blood destruction and partly because of the associated mild hepatic injury which renders it unable to deal with the large quantities of urobilin being reabsorbed from the gut as a result of the excessive formation of bile pigment.

The normal range of fæcal urobilinogen excretion is 40 to 280mgs. per day, usually 100 to 200mgs. The normal range of urinary urobilinogen

is 0 to 4mgs. per day, usually 0·5 to 1·5mgs. In hæmolytic jaundice the fæcal urobilinogen ranges between 300 and 4,000mgs. per day and the urinary urobilinogen up to 200mgs. daily. In parenchymatous jaundice fæcal urobilinogen varies between 0 and 1,000mgs. daily, usually 10 to 300, and the urinary urobilinogen 0 to 300, usually 0·5 to 100, and it depends upon the degree of associated obstruction resulting from rupture of the minute bile canaliculi. These estimations, however, are of particular value for facilitating the differentiation between biliary obstruction due to stone and obstruction due to malignancy of the pancreas or bile duct. Whereas malignant obstruction is complete in 90 per cent. of cases and incomplete in only 10 per cent., the reverse is the case in calculus obstruction. The demonstration, therefore, that an obstruction is complete and persistent over several days is strong evidence in favour of malignancy and vice versa, and the best indication of such completeness or incompleteness of biliary obstruction is to be obtained from simultaneous estimation of fæcal and urinary urobilinogen.

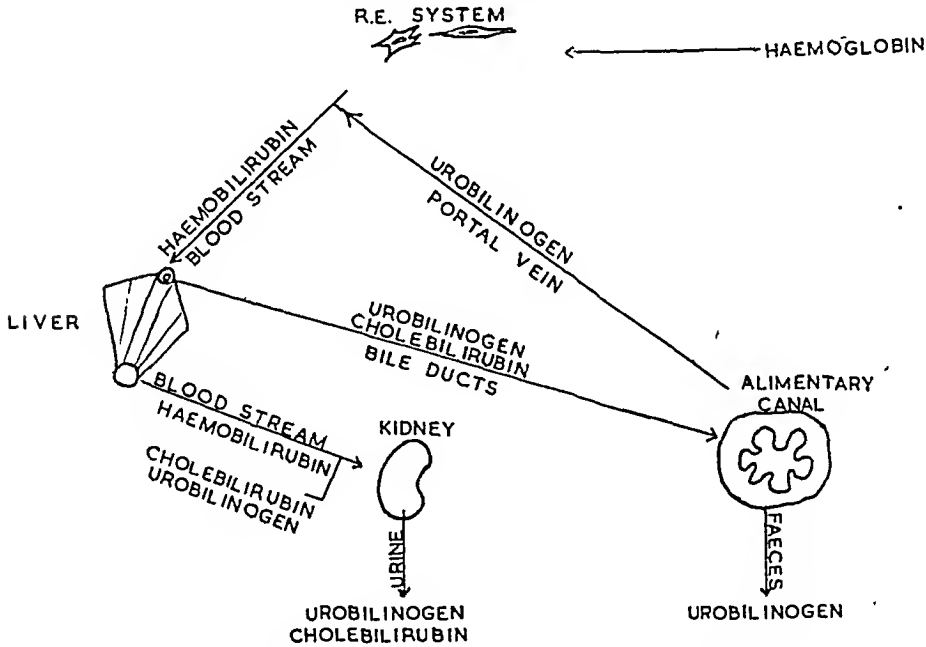



Fig. 1. Diagrammatic illustration of the Circulation of Bile Pigment and Urobilinogen.

## 3. TESTS OF EXCRETORY CAPACITY

A large variety of substances have been used for this type of test. The most frequently employed is bromsulphthalein, of which the dose is 5mg. per kilogram body-weight given intravenously. 85-95 per cent. is removed by the normal liver in five minutes. In the absence of biliary obstruction the test gives useful information of the excretory capacity of the liver. It must, however, be emphasised that impaired hepatic

circulation as in congestive cardiac failure apart from hepatic damage may interfere with the excretion of this dye. Rose Bengal and Azorubin S. have also been used in a similar manner to bromsulphthalein but do not appear to offer any particular advantages. Alkaline phosphatase is normally excreted in the bile and the level of this enzyme in the serum rises considerably in cases of obstructive jaundice. It also rises to a much less extent in cases of parenchymal hepatitis, but it is rare for it to exceed 10 Bodansky units per ml. in such cases. On the other hand, in obstructive jaundice, levels far in excess of 10 units are frequently obtained. Bilirubin itself has also been used as a test substance for assessing the hepatic excretory capacity. 1-1½mgs. of bilirubin per kilogram of body-weight is injected intravenously and the amount remaining in the circulation four hours later is used as an index of liver function. The use of this test is obviously restricted to cases not showing clinical jaundice and its principal disadvantage is its excessive sensitivity.

## 4. TESTS OF METABOLIC AND DETOXIFYING FUNCTIONS

Plasma prothrombin is one of the serum proteins normally synthesised in the liver, but an adequate absorption of vitamin K is essential. As naturally occurring vitamin K is fat soluble, it requires the presence of bile in the alimentary tract for its absorption, and low plasma prothrombin levels therefore may occur in association with liver disease either as a result of biliary obstruction interfering with vitamin K absorption or as a result of parenchymal disease impairing the capacity of the liver to synthesise the protein despite adequate intake of the vitamin. The response to parenteral administration of vitamin K therefore constitutes an admirable test for parenchymal function in those cases where a low plasma prothrombin is found. An adequate response to injection of the vitamin indicates the absence of significant parenchymal damage. Failure of the plasma prothrombin to rise following administration of vitamin K indicates serious parenchymal damage. The capacity of the liver to convert galactose to glucose has also been widely used as a function test. As usually performed 40gms. of galactose are given by mouth and the amount excreted in the urine estimated at half-hourly intervals for three hours. The total should not exceed 3gms. in a normal individual. Owing to variations in absorption from the alimentary canal, an intravenous modification of this test is more reliable. In cases of jaundice the test is of limited differential value if performed within two weeks of the onset of the jaundice, that is before obstruction, if any, has had time to cause much secondary liver damage.

Of the so-called detoxifying functions of the liver the conversion of benzoic acid to hippuric acid by linkage with glycine is the most widely used as a function test. Benzoic acid is administered orally or sodium benzoate by intravenous injection and the excretion of hippuric acid during the next four hours is estimated. The limiting factor is apparently the

ability of the liver to synthesise glycine for coupling with the benzoic acid. The chief criticism of the test is its excessively high sensitivity so that even following a short period of biliary obstruction evidence of parenchymal damage is obtained. It is therefore of very limited value in the differentiation of obstructive and non-obstructive jaundice.

## 5. TESTS BASED ON ABNORMALITIES OF SERUM PROTEINS

As the liver is the organ of synthesis of several of the plasma proteins, it is not surprising that gross quantitative abnormalities are found in association with liver disease. Two principal changes are noticed, a tendency for the albumin progressively to fall and the globulin simultaneously to rise so that in severe cases there is a reversal of the normal albumin globulin ratio. Of the various globulin fractions that may be increased in association with liver disease, the gamma globulin is of outstanding importance and its increase largely responsible for the positive reaction of the so-called flocculation tests. There are at least 10 of these tests available and no doubt others will soon be described, but they are very largely only technical short cuts facilitating the demonstration of increased gamma globulin, particularly if there is an associated fall in the albumin. In employing these tests, however, it must be appreciated that in diseases other than of the liver the globulin fraction may be considerably altered and positive flocculation tests be obtained. Of particular importance in this respect is rheumatoid arthritis.

Of the commonly used flocculation tests the two most popular are those utilising thymol and colloidal gold. As recently shown by Maclagan there is little to choose between these two tests in differentiating parenchymal hepatitis from obstructive jaundice, and as the preparation of the thymol is far simpler than that of the colloidal gold it is to be preferred.

## THE RELATION OF THE RESULTS OF FUNCTION TESTS AND HEPATIC INJURY

Three recent studies have been made of the correlation between the results of the usual function tests and the state of the liver as determined by biopsy (Sherlock, 1946; McMichael, 1948; Franklin, 1948). McMichael has subdivided hepatitis into four grades according to the probable percentage of surviving liver cells. In group (*a*) the surviving liver cells exceed 75 per cent., in group (*b*) they are between 50 and 75 per cent., in group (*c*) between 25 and 50 per cent., and in group (*d*) under 25 per cent. Good correlation was found to exist between the grade thus assessed and the degree of bilirubinæmia and the galactose time (equals the time of disappearance of ·05g. galactose per kilogram given intravenously). No significant difference was found in the serum phosphatase level in any of these four grades. A fall in the albumin globulin ratio was observed to correspond with grade (*c*), and a reversal with grade (*d*). Hippuric acid excretion was found to be impaired with very slight liver

injury and the test is therefore too sensitive to indicate the higher grades of injury. The results of Sherlock and Franklin are fundamentally similar to those of McMichael.

## Conclusion

Properly chosen and conducted liver function tests are undoubtedly of great value as an aid in the differential diagnosis of hepatic disease. It is obvious that there is considerable variation in the usefulness of these tests and of the importance which should be placed on their results in any given case. Whilst it is, of course, impossible and undesirable that any individual subject be exposed to the full battery of these investigations, the minimal adequate investigation of any suspected case of hepatic insufficiency should include the investigation of the urine for bile and urobilinogen, a Van den Bergh reaction on the serum and one reliable flocculation test.

In conclusion it should particularly be noted that a history of a transfusion of blood or serum within the previous two to four months, the presence of spider nævi in the skin, an icteric index exceeding 100 with bile in the stools or a prolonged prothrombin time not responding to vitamin K, strongly suggest the presence of parenchymal liver damage.

## REFERENCES

1 MacLagan, N. F. (1948) *Brit. Med. J.* 2, 892.
2 Sherlock, S. P. V. (1946) *J. Path. Bact.* 58, 523.
3 McMichael, J. (1948) *J. Amer. Med. Ass.* 137, 234.
4 Franklin, M., Popper, H., Steigmann, F., and Kozol, D. D., (1948) *J. Lab. Clin. Med.* 33, 435.

# THE HONORARY MEDAL OF THE COLLEGE

The Honorary Medal of the College was awarded by the Council on May 12 to Professor F. Wood Jones, F.R.S., F.R.C.S., the Sir William Collins Professor of Human and Comparative Anatomy, to Mr. Arthur Sims, the donor of the Commonwealth Travelling Professorship, and to Professor W. E. Gye, M.D., F.R.S., who has been Director of the Imperial Cancer Research Fund since 1935 and will retire in August of this year.

The leading considerations in the award of the Honorary Medal are "liberal acts or distinguished labours, researches and discoveries, eminently conducive to the improvement of natural knowledge and of the healing art." It is the practice of the Council also to cite a special reason when making an award. In the case of Professor Wood Jones it is his important work in Human and Comparative Anatomy, especially in relation to mammalian evolution, and in that of Professor Gye it is his valuable work in the field of cancer research. Mr. Sims is recognised for his great generosity in the endowment of the Arthur Sims Commonwealth Travelling Professorship.

The Honorary Medal is struck in gold and its design shows on the obverse the Arms of the College, and on the reverse Galen contemplating a human skeleton. (For illustration see the *Annals*, vol. 1, facing p. 233.)

## " OBSERVABLES " AT THE ROYAL COLLEGE OF SURGEONS

### 18. THE JACKSONIAN PRIZE

THE JACKSONIAN PRIZE has become the premier award for Fellows and Members of the College aspiring to high places in surgery. From time to time efforts have been made to trace the history of Samuel Jackson, who, in 1800, founded the Prize. It has been known for some time that Jackson was not the patronymic of the donor, and that his birth-name was Orange. He took his wife's name of Jackson when in 1793 he married the daughter of a wealthy ship-broker at Wapping. He then gave up the practice of medicine, took a commission in the Tower Hamlets Militia in which he was eventually promoted to the rank of Lieutenant-Colonel, and sought to attain a prominent social position.

Jackson died in 1825, and in 1835 the Editor of the *Lancet* remarked that he " finally brought a very gay life to a very usual end." The Editor also stated that he had been apprenticed to Henry Cline and that he was probably influenced by him in making his gift to the College. This would have been a romantic connection, for Cline may be regarded as having been the indirect cause of the foundation of the Royal College of Surgeons. It was the irregularity of Cline's election to the Court of Assistants of the Company of Surgeons in 1796 that led to the Act of Incorporation of the Company being voided. A Royal Charter in 1800 established " The Royal College of Surgeons in London." Cline was Master of the College in 1815 and occupied the Chair again as President in 1823.

Recent research by Mr. J. P. Childs, F.R.C.S., of King's College Hospital, has, however, ended this romantic story for he has established that Jackson was in fact apprenticed to William Blizard. The natural surmise is that it was Blizard who interested him in the Royal College of Surgeons and induced him to found and then to endow the prize which bears his name. Mr. Childs finds that in 1835 Mr. William Cooke read a paper on Blizard before the Hunterian Society in which he stated that the prize was " founded at the instance of Sir William by his friend and pupil Samuel Jackson." Mr. Childs has also traced the actual record of Samuel Orange being apprenticed to Blizard in a Minute of the Court of Examiners in 1782 and a further record of his being rebound to Blizard in 1783. Moreover, as Samuel Jackson, he was elected F.R.S. in 1798, being proposed by Basil Hawood and supported by John Heaviside, *W. Blizard* and John Abernethy. In 1787 Samuel Orange was awarded the diploma of M.R.C.S.

The Jacksonian Prize holds pride of place among College awards. Up to the present date the prize has been granted 116 times. One surgeon has won it three times, and seven surgeons have won it twice. It should be encouraging to those who compete for the prize to notice that 33, or 30 per cent., of those who have been awarded it, or have received an honourable mention have later become members of the Council, while 13, or 12 per cent., have become President. Three members of the present Council won the prize and one member received an honourable mention.

W-J.

# THE LIBRARY

## A Representative Exhibition

SOME OF THE CHIEF treasures of the library were exhibited in the Council Room, when a party of the Friends of the National Libraries visited the College last winter. The Friends are a voluntary society, with offices at the British Museum, for promoting the interests and enriching the collections of libraries of national standing. The exhibition illustrated the history of surgery, anatomy, and physiology, and displayed the growth of the College library. Notable examples of fine printing were shown, but the books were chosen primarily for their scientific importance.

The College inherited no books from the Company of Surgeons which it succeeded in 1800, and only 12 from John Hunter's library were presented by his executors when his Museum was placed in the College's care. But already by 1810 a collection was being formed, when the Council agreed that "examples of ancient writers should be especial objects of munificence." The library was organised in 1827, and Robert Willis, M.D., a notable scholar, was appointed the first librarian. He did much to make the collection representative of the classics of medicine of all periods. When the College was rebuilt in the 1830s it was recorded in the minute-book that "one great object in rebuilding was to have a library in which the books might be accessible." The reading-room then designed by Sir Charles Barry is one of the finest in London. The library at that time numbered about 20,000 volumes. Fifty years later, during its most active period under James Blake Bailey, who was called "a prince of librarians," it had doubled its extent, and to-day it is more than twice as large again.

The library was originally designed to supplement the Hunterian Museum displaying John Hunter's study of living processes, whose maintenance and repair is the purpose of surgery. Its first service has always been to the scientific staff of the College, which has included anatomists as famous as Sir Richard Owen and Sir William Flower. At the same time the Council has administered it in a liberal spirit, making it freely open to all serious readers introduced by Fellows or Members. In particular it provides for the needs of post-graduate students attending the College's courses of instruction.

The first group of exhibits centred on the work of John Hunter. Here were shown Hunter's own manuscripts which survived the holocaust of 1823, books printed at his private press, and drawings made for him. Beside them were books by his teachers William Hunter and Percivall Pott, including the autograph manuscript of Pott's book on hydrocele (1766), and by his pupils, Abernethy, Astley Cooper and Jenner.

Anatomy was represented by illustrated books chiefly of the Renaissance period, from the scientifically primitive woodcuts of Ketham (1495), Beregario (1522) and Estienne (1545 and 1546) to the magnificent illustrations in the *De fabrica* of Vesalius (1543 and 1555) and their copper-plate adaptations in the English and French editions of Geminus (1545 and 1564).

The books of comparative anatomy included such rarities as the *Figure anatomiche* of Germano (1625), the first *Descriptions* by Perrault (1669) of animals dissected at the Académie des sciences in Paris, and Edward Tyson's *Anatomy of a pygmy* (chimpanzee) 1699.

The surgical group was marked by many sixteenth century books. Two of Ambroise Paré's original texts were shown, the *Dix livres de chirurgie* 1564 and the *Cinq livres* 1572. Other continental surgery books included Pierre Franco *Traité des hernies* 1561, Paracelsus *Wundarzney* 1561, and Guillemeau's *Chirurgien françois* 1594 with the English translation 1597. The four English editions of Vigo's *Works of chirurgerye* were exhibited, with William Clowes *Proved practise* bearing an inscription by Dr. Richard Foster who is mentioned in the text. With these were other rare Tudor books: Elyot's *Castel of helthe* 1541 and Borde's *Breviary of health* 1547, and Monardes *Joyfull news out of the new-found world* (1580), showing one of the earliest pictures of the tobacco plant, with the Spanish original (1574).

Seventeenth century surgery was represented by John Woodall's *Surgeon's mate* 1639, with the engraved equestrian portrait of King Charles I, a copy which bears the signature of Charles Bernard, serjeant surgeon to Queen Anne. Bernard's library catalogue was alongside, showing that this copy of Woodall was sold for 2s. in 1711. Richard Wiseman's *Treatise of wounds* 1672 was also shown, with various editions of his *Chirurgicall Treatises.*

The section on physiology lead from Jean Fernel's *Physiologia* of 1554 to the early papers (*circa* 1890) of Santiago Ramon y Cajal on the histology of the nervous system. Here were shown Gaspare Aselli's book on the lacteals (1627) with the first coloured woodcuts ever used in a medical book, the first edition of William Harvey's *De motu cordis* 1628, and Christopher Wren's drawings of the nervous system illustrating Thomas Willis on the anatomy of the brain 1664. Fabricius of Acquapendente on the organs of special sense (1600) was followed by Descartes on Man (Latin 1662, French 1677) with its diagrams of the optic nerves, and Newton's *Optics* 1704. Arruga on detachment of the retina 1936 was exhibited as an example of a modern ophthalmic book with fine colour-printed plates.

Contributions from the staff of the College included Richard Owen's *Odontography* (1840-45) with its unsurpassed illustrations of dental histology, Robert Willis's translation of Harvey's works 1847, and some of Sir Arthur Keith's anthropological books with measured cranial drawings (1931 and 1939).

A group of early periodicals, all from the end of the seventeenth century, included the Italian *Accademia del Cimento*, the Dutch *Observationes anatomicae*, the French *Zodiacus medico-Gallicus*, and the English *Medicina curiosa.*

Among the manuscripts were the fifteenth century Woman's book with obstetric illustrations, original letters of Herman Boerhaave and B. S.

Albinus, Hunter's letters to Jenner, Jenner's essay on cowpox, Pasteur's letters to Lister, and Lister's notes of his experiments on moulds including penicillium (1871). Dr. John Arbuthnot's letter-book was also shown.

Books which recorded special advances in medical science included Laennec on the stethoscope 1819, Beaumont on the gastric juice 1833, Florence Nightingale's *Notes on nursing* 1859, and Roentgen on " a new kind of rays " 1895—all original editions.

A few fine bindings from the sixteenth to the eighteenth century were shown, and a dozen engraved portraits of medical men, the work of such master engravers as Bartolozzi, Basire, Earlom, Vertue, and Valentine Green.

## MONTHLY DINNERS

Monthly dinners are held in the College on the Wednesday before the second Thursday of each month. The following are entitled to attend with their guests. All Diplomates and students of the College, and Members of the Associations linked to the College through the Joint Secretariat. It is not necessarily intended that guests should be members of the medical profession.

The dinners will be at 7 p.m. on the following Wednesdays: July 13, October 12, November 9, and December 7, 1949, January 11, February 8, March 8, April 12, May 10 and June 7, 1950. There is an inclusive charge of £1 5s. (including drinks), which must be sent with the application to the Assistant Secretary at least a week before the date of the dinner. The dress is Lounge Suit or Uniform.

## DIARY FOR JUNE (15th-30th)

| | | |
|---|---|---|
| Wed. 15 | 3.45 | Prof. H. A. Magnus—Gastric Cancer. |
| | 5.00 | Dr. D. J. Bell—Carbohydrate Metabolism. |
| Thur. 16 | | First Membership Examination, Final L.D.S. Examination—(Part II), and D.P.M. Examination (Part II) begins. |
| | 3.45 | Dr. D. J. Bell—Carbohydrate Metabolism. |
| | 5.00 | Prof. J. Z. Young—Nerve Repair. |
| Fri. 17 | | D.L.O. Examination (Part II) begin. |
| | 3.45 | Dr. H. L. Marriott—Water and Electrolyte Balance. |
| | 5.00 | Prof. J. Z. Young—Nerve Repair. |
| Mon. 20 | 3.45 | Dr. H. L. Marriott—Water and Electrolyte Balance. |
| | 5.00 | Prof. Lord Stamp—Principles of Immunity in Relation to Surgical Practice. |
| Tues. 21 | 3.45 | Lt.-Col. W. H. Hargreaves—Antibiotics. |
| | 5.00 | Prof. Lord Stamp—Some Practical Applications of Bacteriology to Surgery. |
| Wed. 22 | 3.45 | Dr. Michael Kremer—Visceral Sensation. |
| | 5.00 | Mr. Sol. M. Cohen—Traumatic Arterial Spasm. |
| Thur. 23 | 4.00 | Prof. A. Kekwick—Nutrition and the Surgeon. |
| | 5.15 | Mr. R. W. Reid—Disordered Renal Function: the Surgeon's Point of View. |
| Fri. 24 | | L.D.S. Examination (General and Special Anatomy and Physiology) and D.P.H. Examination (Preliminary) begin. |
| | 3.45 | Prof. A. Kekwick—Nutrition and the Surgeon. |
| | 5.00 | Mr. R. W. Reid—Disordered Renal Function: the Surgeon's Point of View. |
| Mon. 27 | 5.00 | Dr. M. Ravitch—Anal Ileostomy with Sphincter Preservation in Patients requiring Total Colectomy for Benign Conditions.* |
| Tues. 28 | | Final Membership Examination begins. |
| | 2.00 | Imperial Cancer Research Fund Council. |
| Wed. 29 | 5.00 | Prof. Sir Horace Evans—Hunterian Lecture—Hypertension.* |
| Thur. 30 | | D.P.H. Examination (Final) begins. |
| | 5.00 | Prof. Arnold Sorsby—Streptomycin in Ophthalmology.* |

* Not part of courses.

# DIARY FOR JULY

| | | | |
|---|---|---|---|
| Mon. | 4 | 2.30 | MR. T. TWISTINGTON HIGGINS—Children as Surgical Patients. |
| | | 4.30 | MR. D. LEVI—Congenital Pyloric Stenosis. |
| | | 5.00 | PROF. R. HARE—General Principles of Immunity and Infection (Part I). |
| | | 6.15 | Dental Lecture. |
| Tues. | 5 | 2.30 | MR. J. H. DOGGART—Ocular Clues to the Diagnosis of Extra-ocular Diseases. |
| | | 5.00 | MR. GORDON MURRAY—Moynihan Lecture: Congenital Heart Disease.* |
| | | 5.00 | PROF. R. HARE—General Principles of Immunity and Infection (Part II). |
| | | 6.15 | Dental Lecture. |
| Wed. | 6 | 2.30 | MR. D. F. ELLISON NASH—Some Urinary Affections of Children. |
| | | 4.30 | MR. F. DOUGLAS STEPHENS—Hirschsprung's Disease. |
| Thur. | 7 | 11.00 | Election to Council. |
| | | 2.30 | MR. R. H. FRANKLIN—Congenital Atresia of the Œsophagus. |
| | | 4.30 | MR. R. SCOTT MASON—Congenital Abnormalities of the Rectum. |
| | | 5.00 | Dental Lecture. 6.15 Dental Lecture. |
| Fri. | 8 | | D.O.M.S. Examination (Part I) begins. |
| | | 2.30 | MR. J. CROOKS—Laryngoscopy and Broncoscopy in Childhood. |
| | | 4.30 | MR. D. N. MATTHEWS—Hare Lip and Cleft Palate. |
| Mon. | 11 | 5.00 | PROF. R. HARE—General Principles of Immunity and Infection (Part III). |
| | | 6.15 | Dental Lecture. |
| Tues. | 12 | 5.00 | PROF. R. HARE—General Principles of Immunity and Infection (Part IV). |
| | | 6.15 | Dental Lecture. |
| Wed. | 13 | 5.00 | MR. NORMAN S. SHENSTONE—Tudor Edwards Lecture—The Treatment of Bronchiectasis.* |
| | | 7.00 | *Monthly Dinner for Fellows, Members, Licentiates, Diplomates and Students of the College, and Members of the Associations in the Joint Secretariat* (*see page* 403). |
| Thur. | 14 | | Primary F.R.C.S. Examination begins. |
| | | 2.15 | Election of President and Vice-Presidents. |
| | | 5.00 | PROF. JOHN BEATTIE—Bernhard Baron Lecture: Adventures in Metabolism.* |
| | | 5.00 | Dental Lecture. 6.15 Dental Lecture. |
| Fri. | 15 | | Board of Faculty of Dental Surgery. |
| | | | D.O.M.S. Examination (Part II) and D.I.H. Examination (Part I) begin. |
| | | 11.00 | Faculty of Dental Surgery Elections. |
| | | 3.00 | Faculty of Dental Surgery Elections. |
| | | 3.00 | Annual General Meeting of Faculty of Dental Surgery. |
| | | 3.45 | PROF. KURT THOMA—Charles Tomes Lecture, Part I: Odentogenic Tumours of the Jaws.* |
| | | 5.00 | PROF. KURT THOMA—Charles Tomes Lecture, Part II: Osteogenic Tumours of the Jaws.* |
| | | 8.00 | Second Anniversary Dinner of the Faculty of Dental Surgery. |
| Mon. | 18 | 5.00 | DR. G. J. CUNNINGHAM—General Pathology of Tumour Formation (Part I). |
| | | 6.15 | Dental Lecture. |
| Tues. | 19 | 5.00 | DR. G. J. CUNNINGHAM—General Pathology of Tumour Formation (Part II). |
| | | 6.15 | Dental Lecture. |
| Thur. | 21 | | D.T.M. & H. Examination begins. |
| | | 5.00 | Dental Lecture. 6.15 Dental Lecture. |
| Fri. | 22 | | D.I.H. Examination (Part II) begins. |
| | | 9.00 | Reception to Fourth International Congress of Otolaryngology. |
| Mon. | 25 | 5.00 | DR. G. J. CUNNINGHAM—General Pathology of Tumour Formation (Part III). |
| | | 6.15 | Dental Lecture. |
| Tues. | 26 | 5.00 | DR. G. J. CUNNINGHAM—General Pathology of Tumour Formation (Part IV). |
| | | 6.15 | Dental Lecture. |
| Thur. | 28 | 5.00 | Dental Lecture. 6.15 Dental Lecture. |

* Not part of courses.

# INDEX TO VOLUME 4


Page

ADAIR, F. E.: Surgical problems involved in breast cancer .. 360
Anæsthetists, Faculty of .. .. 213
Arms of the Company and College 257

BADENOCH, A. W.: Congenital obstruction at the bladder neck 295
Bladder neck. congenital obstruction at the .. .. .. .. 295
Bradshaw lecture for 1948 .. .. 65
Breast, female, and its development 317

CADE, Sir Stanford: Malignant disease of the mouth .. .. 381
Cancer, surgical problems involved in breast .. .. .. 360
CAPPS, F. C. W.: Malignant diseases of the paranasal sinuses .. 38
Carcinoma of the pancreatoduodenal area, surgical treatment of 197
CATTELL, R.: Surgical treatment of carcinoma of the pancreatoduodenal area .. .. .. 197
CAWTHORNE, T.: Some observations on the pathology and surgical treatment of labyrinthine vertigo of non-infective origin 342
Clover, Joseph Thomas, life and achievements of .. .. 267
COPE, V. Z.: John Hunter's account of a "Mortifyd" appendix caeci 142
Cowell, Sibert Forrest .. .. 121
Cysts in general, Zeis's gland and sebaceous .. .. .. 58

DEVELOPMENT, early stages of human .. .. .. .. 281
Diary 63, 64, 125, 194, 195, 265, 266, 335, 336, 403, 404
Dinner, Hunterian .. .. .. 164
Dinners, monthly 63, 125, 194, 265, 335, 403
DODDS, E. C.: Pathological and physiological aspects of sterol metabolism .. .. .. 104
DUKES, C. E.: Observations on the appearances of intestinal tumours .. .. .. 24
— Surgical significance of the unusual in the pathology of intestinal tumours .. .. 90

Page

ESNAURRIZAR, M. L.: Surgical relief of abdominal paid by splanchnic block .. .. 192
Exhibition, a representative .. 401

GIRDLESTONE, G. R.: Pott's disease and Pott's paraplegia .. 214
GLYNN, L. E.: Liver function tests 392

HAMILTON, W. J.: Early stages of human development .. 281
Head injury, pathology of .. .. 232
— problem of closed .. .. 308
Hunter, John, and his museum .. 337
— the observer .. .. .. 127
Hunterian dinner .. .. .. 164
— lectures .. .. 168, 295, 342
— oration for 1949 . .. .. 127
Hunter's, John, account of a "Mortifyd" appendix caeci .. 142
— writings .. .. .. .. 123

IMPERIAL Cancer Research Fund lecture .. .. .. .. 90

JACKSONIAN Prize .. .. 400
Jenner, Edward .. .. .. 332
Jones, F. Wood: John Hunter and his museum .. .. .. 337

LIBRARY .. .. 123, 261, 332, 401
Lister, Vesalius and.. .. .. 261
Liver function tests .. .. .. 392

MANDIBLE, osteomyelitis of .. 48
MARSTON, A. D.: Life and achievements of Joseph Thomas Clover 267
Medal, honorary, of the College .. 399
Metabolism, pathological and physiological aspects of sterol 104
—s, disordered, in thyrotoxicosis and myxœdema .. .. 3
Mouth, malignant disease of the .. 381
Moynihan lecture .. .. .. 360

NELSON'S wounds, records of Admiral Horatio .. .. 326
NORBURY, L. E. C.: Bradshaw lecture for 1948 .. .. 65

Page

"OBSERVABLES" at the Royal College of Surgeons 60, 122, 160, 257, 326, 400

PAIN, facial .. .. .. 206
Pott's disease and Pott's paraplegia 214
Prize, Jacksonian .. .. .. 400
Proctology throughout the ages .. 65

RESIDENTIAL quarters, opening of .. .. .. .. 328
Restoration and development fund 121, 141, 260, 280, 380
ROBERTSON, J. D.: Disordered metabolisms in thyrotoxicosis and myxœdema .. .. 3
ROWBOTHAM, G. F.: Problem of closed head injury .. .. 308
Rowlandson water-colours.. .. 122

SAYINGS of the great 23, 98, 143, 212, 307, 380
SIMPSON, K.: Pathology of blunt head injury .. .. .. 232
Sinuses, malignant diseases of the paranasal .. .. .. 38
SMITHERS, D. W.: High voltage X-rays in the treatment of malignant tumours at a depth 242
SOUTTAR, H. S.: Hunterian oration for 1949 .. .. .. 127
Splanchnic block, surgical relief of abdominal pain by .. .. 192

Page

Statuette, a bronze écorché .. 60
Stubbs, George, R.A., pictures by 160
SYMONDS, Sir Charles: Facial pain 206

TAYLOR, J.: Wilfred Trotter .. 144
Trotter, Wilfred .. .. .. 144
Tuberculosis, observations on the pathogenesis and treatment of skeletal .. .. .. .. 168
Tumours at a depth, high voltage X-rays in the treatment of malignant .. .. .. 242
—, observations on the appearances of intestinal .. .. .. 24
—, surgical significance of the unusual in the pathology of intestinal .. .. .. 90

VERTIGO, some observations on the pathology and surgical treatment of labyrinthine, of non-infective origin .. .. 342
Vesalius and Lister .. .. .. 261

WASS, S. H.: Osteomyelitis of the mandible .. .. .. 48
WEST, C. M.: Female breast and its development .. .. .. 317
WILKINSON, M. C.: Observations on the pathogenesis and treatment of skeletal tuberculosis .. 168
WOLFF, E.: Zeis's gland and sebaceous cysts in general .. 58